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VOL. VI FEBRUARY, 1911 No. 1

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WITH 21 PLATES, 5 FIGURES, 15 CHARTS, 3 DIAGRAMS, AND 2 MAPS.

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VOL. VI FEBRUARY, 1911 No. 1

NUTRITION AND GROWTH: I.

By HANS ARON.
(*From the Physiological Laboratory, Philippine Medical School, Manila, P. I.*)

CONTENTS.

INTRODUCTION. Present knowledge of the relation between growth and nutrition. The problem.
DESCRIPTION OF EXPERIMENTS. Methods, especially those used in the chemical analysis of the animals. Four sets of experiments on 14 dogs.
DISCUSSION OF EXPERIMENTS.
  Influence of a restricted diet on growing dogs.
    Effect on the weight and appearance of the animals.
    Relative amount of change in certain parts of the body as compared with other parts.
    Changes in the chemical constitution of the body.
    Energy requirement and food consumption.
  Biological considerations concerning the suppression of growth by restricting the food.
  Energy required during growth.
  The increase in weight as an index to growth, with special reference to children.
CONCLUSIONS.

INTRODUCTION.

As all the newly formed materials of the body are derived from the ingested food, nutrition must be one of the most important factors influencing the process of growth. Therefore, it is obvious that an intimate study of the relationship between nourishment and growth will furnish a valuable addition to our general knowledge of the physiology of growth.

The question of the influence of food on the process of growth is by no means merely theoretical. It has an important bearing on practical problems also, for the study of nutrition in modern pediatrics is gaining steadily in importance and much evidence has been accumulated showing how closely food and development are related. Only a thorough knowledge of the physiologic conditions of the process of growth and of its relation to nutrition can furnish a scientific basis for the feeding of infants as well as a clear insight into the problems involved.

Rubner,[1] during the past two years, has published extensive studies concerning the relationship of growth and nutrition. I have followed his ideas as closely as possible in my introductory discussion and I shall use his terminology, or the English equivalents, in preference to that which I employed in a paper[2] on the same subject written before his publication appeared. It is not my intention to discuss Rubner's fundamental work; nor his demonstration that the problem of the duration of life is involved in that of the number of calories metabolized during life. His theory that man, in contrast to all other mammals, occupies a particular position probably will not hold against the objections made by other authors.[3] However, Rubner's treatment of the fundamental questions concerning the application of the laws of energy to the problem of growth furnishes the basis for all considerations and investigations of this subject.

The original cause of the process of growth is the "capability of growing," as I have called it, or, better, the "tendency to grow," the term used by Rubner. While we are fairly well informed concerning the morphology of this process, its biology is dark. The "tendency to grow" results from the tendency of the juvenile cells or the cells in the juvenile organism to divide and to multiply. This tendency is strongest in the very young animal; it gradually becomes less marked, and finally is lost when the organism has grown enough; i. e., has passed the period of youth and become an adult. An adult organism under certain conditions may increase in certain parts of the body, but these processes known as "hypertrophy" (called forth by an increased demand of work on the muscles, heart, kidneys, etc.) or "pathologic growth" (tumor) are markedly different from that which we term "growth" in the sense of development.

The "tendency to grow" has an upper limit. This means that more than a certain quantity of new tissue can not be produced under any circumstances. This upper limit is variable, not only for the same individual according to the stage of development or age, but also in different individuals of the same species and especially in different species of animals. The rabbit and the dog have an upper limit which is very high, that is, these animals have a great "tendency to grow," while the human has only a small one.

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[1] *Arch. Hyg.* (1908), **66**, 1–208; Kraft und Stoff im Haushalte der Natur, Leipzig (1909), 116–17.

[2] *Biochem. Ztschr.* (1908), **12**, 28–77.

[3] Hans Friedenthal, *Verhandl. d. physiol. Gesellschaft*, Berlin (1909), 93, and (1910), 22.

The process of growth depends, not only upon this "tendency to grow," but also on the food. The "tendency to grow" induces the normal production of new tissues only when the material necessary for the construction of these new tissues is furnished by the food. The quantity of growth, to the upper limit of this tendency, is determined by the food. Rubner expresses the same idea when he says that "nutrition has a moderating influence on the process of growth." Therefore, the rate of growth depends upon two factors, the "tendency to grow" and the nutriment. Rapid growth takes place if this tendency is high in the cells and a sufficient quantity of food is taken to furnish all the substances needed. If there is no such tendency, then even the maximum intake of food will not lead to growth. It would naturally be expected that the converse should also be true; in spite of a high "tendency to grow" no growth should take place if the substances needed for this growth are not present in the food.

We must apply the laws of energy in studying the influence of nourishment on growth. From this point of view a growing animal requires food for two purposes: first, like the adult, to replace the energy expended in the production of heat and the work of the vegetative organs; and, second, for the formation of new body substances. This division of the needs of a growing animal into (1) energy required for maintenance and (2) energy required for growth, seems to be logical and it is adopted by the most competent authors dealing with this subject.[4]

The intake of energy, in order to enable an organism to grow, must exceed the requirement for maintenance, and this excess of energy is used for the formation of new body substances. However, in this instance it is not simply a question of energy in the form of calories; the protein intake also must exceed the demand for wear and tear and the excess of protein is stored in the form of new body cells. Similar considerations apply to certain inorganic constituents of food. Since the excess over the requirement for maintenance alone will be used in the formation of new body substances, the amount of growth will depend on the amount of this excess.

A further deduction leads to the conclusion that no growth will take place if there is in the food no excess over the amount of energy required for maintenance. In other words, it should be possible, by a proper restriction of the food, to suppress all growth. This conclusion has been accepted frequently without question. Gerhartz,[5] for example, regarded the requirement for maintenance of young dogs as equal to the caloric intake during periods in which the weight of these dogs neither increased nor decreased.

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[4] *Ostertag und Zuntz, Landwirtsch. Jahrb.* (1908), **37**, 211.

[5] *Biochem. Ztschr.* (1908), **12**, 97–118.

Will growth, suppressed by the necessary restriction in diet, cease entirely for an indefinite length of time? What becomes of an animal, suffering such a suspension of growth, when it is given an abundant food supply?

Rubner[6] states as follows in regard to these questions:

> If the cells of a young animal are insufficiently nourished, the growth does not proceed. There is also no decrease of the energy metabolism (under which circumstances a decrease of the body temperature could not be avoided), but growth stops, without there being a loss of the "tendency to grow" in the near future. He bases this idea on experiments performed by O. Kellner with the silkworm and upon the work of Quetelet, who found the individuals of the working class to be smaller in stature than those of the better classes.

I shall here quote from the investigation of Kellogg and Bell[7] on the influence of diminished nourishment on silkworms (*Bombyx mori*).

> These authors state that "there exists a very definite and constant relation between amount of food and size as indicated by weight, the starveling individuals being consistently smaller than the well-nourished, the lingering effects of this dwarfing being handed down even unto the third generation, although the progeny of the famine generation be fed the optimum amount of food. In case the diminished nourishment is imposed upon three or even two successive generations there is produced a diminutive, but still fertile, race of Lilliputian silkworms whose moths, as regards wing expanse, might join the ranks of the micro-Lepidoptera almost unremarked.
>
> "An abnormal extension of the time needed for the metamorphosis follows upon a reduction of the food supply."

After my experiments were nearly finished and reported in part at the Far Eastern Association for Tropical Medicine in March,[8] 1910, there came to my attention, through the courtesy of Geheimrat Zuntz, a paper by H. F. Waters,[9] which deals with a problem similar to mine, but considered principally from the standpoint of animal husbandry.

> This author reports on experiments on cattle which were fed with widely different quantities of food, in order to cause in some a normal gain in live weight (full fed); in others a fair growth but without allowing fat to be stored up (moderately fed); in still others only a slight gain in live weight (retarded development). In another group the feeding was so conducted as to allow of no increase in live weight (maintenance), and in a last group the animals were fed so as to lose in live weight (submaintenance). Waters has carefully studied the build of these animals, their size, and the size of their different parts. His results will be discussed in detail later in connection with my own.

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[6] *Arch. Hyg.* (1908), **66**, 1–208; Kraft und Stoff im Haushalte der Natur, Leipzig (1909), 116–117.

[7] *Science*, (1903), **18**, 744, 746.

[8] *Berl. klin. Wchnschr.* (1910), 993.

[9] The influence of nutrition upon the animal form. XXX. Meeting of Society for the Promotion of Agricultural Science.

In view of the preceding considerations, it seemed quite interesting and promising thoroughly to study the influence of variations in the quantity of food, and more especially of a restricted diet, on the growth and development of mammals.

To solve this problem, we must first study the conditions surrounding the suppression of growth when the animal is at a standstill, receiving only the amount of food required for existence without growth. We must further endeavor to determine the maximum quantity of food which can be given without causing growth, and in what way varying additional amounts of food are used in the formation of new body substances.

A number of questions at once arise. Can we, by the restriction of food, suppress the process of growth entirely and, if so, for how long? If we suppress the growth, does the animal lose its "tendency to grow" as it ages? Does the capability for growing depend on the age, or on the size and weight of the animal? Is the growth of all parts of the body suppressed to the same degree, or is the "tendency to grow" of the various parts or organs of the body different? Do some parts develop or grow at the expense of the rest? It is known that in a starving animal the most important parts of the body, such as the heart and brain, suffer relatively much less loss in weight than do those of minor vital importance, namely, fat, muscles, and digestive glands. If different parts of the body do have a marked difference in the "tendency to grow," we shall be able to recognize this difference by suppressing the growth for a time.

The simplest and most usual method of estimating growth is by controlling the live weight. A constant increase in weight is conclusive evidence of the normal growth of a young animal. Some other indications of growth are increase in length and in other dimensions and certain changes which relate to the stage of development.

If the body weight remains constant, does this fact indicate that no growth is taking place? Growth, as we understand it from a biologic standpoint and in its relation to energy, constitutes a general, more or less equal, increase of all parts of the body. No growth means no change whatsoever in the body.

However, the live weight of an animal may not change at all, while internal relative "changes between the different parts of the body," of which I have already spoken, may take place. Obviously a constant live weight is not an indication of lack of growth in our sense. The question as to how far increase or constancy of live weight runs parallel with growth or cessation of growth is important and of practical value and deserves close attention. On the basis of these considerations the experiments to be undertaken may be outlined as follows.

A number of comparable animals must serve for each series of experiments, one of them receiving just enough food to keep its body weight constant, the others, varying additional amounts so that a more or less intensive growth results. The work must include a careful control of the intake of food, of the body weight, and of the growth. Several difficulties are encountered in determining the latter. It is obvious that metabolism experiments are not suitable for this purpose, even if the respiratory metabolism be included. Such experiments, if extended over a long period, might reveal the total loss or gain of the body in certain substances, but would give no information concerning the behavior of the different parts and organs. What we really wish to know is the composition of the body at the beginning and at the end of the experiment.

A detailed analysis of the body appeals to me as the best method of gaining this information. Of course, we can not analyze the same animal twice. We can only determine its composition at the end of the experiment, and in order to secure data concerning the probable composition at the beginning we can either analyze a comparable control animal or find the composition by calculation from data obtained on other normal animals.

My experiments have been confined to dogs. A medium-sized dog is easy to handle, but large enough to permit a careful study and analysis of the different parts and organs of the body with a fair degree of accuracy.

DESCRIPTION OF EXPERIMENTS.

The general methods adopted were the following:

The animals were placed in a quarantine stable for from one to four weeks and the intestinal parasites, with which practically every dog in the Philippine Islands is infested, removed.[10] To this end, I gave from 0.5 to 1 gram of thymol by mouth daily for a period of from seven to ten days. Following this the dogs were allowed to become accustomed to their food and were all brought into a similar condition as to nutrition.

After this preparatory treatment, the animals were transferred to the experimental stable. This was a large, airy room constructed under an old wooden building with a wire fence on one side.[11] Four to six animals had at least 20 square meters of space and were fairly well protected from the sun and rain. Once or twice in the typhoon season they experienced a good drenching. The floor of the stable was nearly 2 meters above the ground and was constructed of small parallel boards with intervening spaces of about 1 centimeter to allow water to flow away easily. The room was cleaned every morning by flooding and once or twice each week it was disinfected with carbolic acid.

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[10] It has not been proved that parasites influence the metabolism in a marked degree, but in other experiments dogs on a low diet became emaciated and died and their intestines contained numerous ascarides and tæniæ. I am inclined to believe that weak, poorly nourished animals suffer from these parasites.

[11] Only two dogs (A and B) which were kept considerably longer, since September, 1910, were placed in large metabolism cages in the animal house of the new laboratory building.

The food was prepared fresh every day, or every second day. The foods used were rice, canned condensed milk, sugar, and, later, commercial corn starch and meat. The meat was obtained fresh from cold storage; the fat was cut away and the rest passed through a grinder. Each food material was weighed and boiled with water in a weighed pot after adding sodium chloride or other salt mixtures. After cooling, water was added to a certain weight, the mixture stirred carefully, and the portion for each animal weighed. At the same time 50 or 100 grams of the mixture were placed in a large, well-closed jar with formalin until food specimens for twenty-five or fifty consecutive days were collected. These mixtures were used for analysis. Only meat and starch were fed to the animals during the greater part of the experiments.

The mixture at the beginning consisted of 1 part of starch and 10 parts of meat; later of 1 part of starch and 2.5 parts of meat. One hundred grams of food therefore consisted of 40 grams of meat; 16 grams of starch; and 44 grams of water and salts.

The animals were fed every forenoon between 9 and 10 o'clock. Each dog was transferred to a small cage and kept there until it had finished eating. During the first few weeks, it was necessary to give the food in two portions. After that period every dog ate his entire amount in from five to ten minutes.

The animals were weighed every one or two days before being fed, in order to have an exact control of their body weights as an indication of growth or of cessation of growth. The weights are recorded at intervals of five days so as not to make the tables too cumbersome. I have also prepared charts showing the weight of the animals and the amount of food administered at successive intervals.

At the conclusion of an experiment the entire animal was analyzed. The main object was to determine the weight and composition of the different parts of the body; particularly the percentage of the important constituents such as water, protein, and fat.

Dissection had to be done very quickly in order to avoid the rapid decomposition due to this climate. After the weight of the fresh material had been determined formalin was added. Formalin, while rendering work with the material rather disagreeable, nevertheless served admirably as a preservative and in no way affected the accuracy of the results of the analyses. It is a safe disinfectant, does not contain inorganic constituents, and can be removed readily by evaporation.

As a rule, it is very difficult to grind elastic or connective tissue in mills or grinders, even if the tissue is well dried. After being in contact with formalin it becomes hard and brittle. The formalin method effects the same result, therefore, as the more complicated one of freezing the tissues and passing them through a special grinder. By using formalin it is easy in a few hours to grind thoroughly in a small meat grinder the entire body of a dog weighing 5,000 grams.

In the first experiment the animals were killed with ether, but in the later ones by cutting the large blood vessels of the neck, the blood being collected in a weighed porcelain dish; then the body was placed in a large tared dish and the weight noted. The abdomen was opened and the gastro-intestinal tract ligated at the cardia and the rectum, and removed; the weight of the whole tract with the contents intact was taken. Following this the stomach and intestines were opened, the contents removed, and the gastro-intestinal tract cleaned and weighed again. Now organ after organ was separated, weighed (the necessary cross-sections being made to exclude gross pathologic changes), and placed with the others in a weighed, salt-mouthed bottle which was closed air-tight by means of a sheet of rubber and a wire fastener. Then from 40 to 50 cubic centimeters of

40 per cent formaldehyde were added, the bottle closed and weighed again. In the first experiment, the water content of each organ was determined.

The blood from the large vessels, the heart, lungs, and other organs was collected in a dish, which was weighed at the end of the experiment, after a known amount of formalin had been added. A part of this blood-formalin mixture was preserved in an air-tight bottle.

The skin was carefully removed, all subcutaneous fat being left behind. As yet no detailed analyses of the skin have been made.

The brain was removed, weighed, and kept with formalin in the manner just described.

A more exact analysis of the bones seemed advisable in the course of the later experiments, and a number of bones were carefully freed of all flesh and other adhering parts. This waste material was carefully collected. The cleaned bones were weighed and again preserved with formalin in a closed bottle.

At this time about three hours may have elapsed since the death of the animal. The remainder of the body, without skin, blood, organs, brain, and perhaps certain bones, was weighed again and then cooked with a fair amount of water in a large, weighed pot for from one to two hours. Following this operation the meat and bones were separated with forceps and knife, the juice being left with the meat. This separation generally required about half a day. Formalin was then added to bones and meat. The weighings were accurate to 1 gram. The bones were weighed on a large analytical balance, accurate to 0.1 gram.

In experimenting with a trial animal, I added formalin before separating bones and meat, but this procedure is not to be recommended, as the tissues around the bones become so hardened that it is almost impossible to remove them.

The bones preserved with formalin were dried on a hot day by exposure to the sun on a large plate from morning to afternoon and the weight of the air-dried bones was determined.

The meat, juice, and formalin were evaporated to the consistency of porridge, the total weight was determined, and the mixture placed in air-tight bottles.

Both bones and meat, after they have been treated with formalin, retain so much of this preservative that they are protected against decomposition. The entire animal, after all the above processes have been accomplished, is well preserved and contained in eight or ten handy bottles, so that it may be analyzed at leisure.

The organs and the meat of the body are passed several times through a sausage-meat grinder before analysis. Care must be taken not to lose any of the fluid; but even if there is much of this before grinding, it is completely absorbed afterwards. No appreciable loss occurs if the grinding is done quickly and the grinder then carefully cleaned. Several times I weighed organs before and after grinding and found a loss of only 3 to 4 grams per kilo, which is of no importance. Moreover, in our calculations, we assume that the total amount of organs, meat, brain, etc., is the weight of those materials before being subjected to the grinding process. We know the weight of the fresh organs. The formalin added being absolutely volatile, we can determine solids, as well as fat, protein, ash, etc., in the preserved materials and from these data we can calculate the composition of the original, fresh substance.

A difficulty in determining the weight of the entire skeleton arose from the fact that the bones were divided into two parts, one cooked, the other uncooked. It is not necessary to do this, but it seemed advisable in some instances. Only such bones as occur in pairs in the body had been removed and analyzed separately before the rest were cooked. Hence it was only necessary to weigh the cooked bones which corresponded to those previously set aside and add this weight to the total in order to obtain the weight of the entire cooked skeleton. A slight error is involved in this process because the extract of the cooked bones is left with the meat. Another difficulty arises in the attempt to calculate the water content of the fresh meat and the fresh skeleton. We know the total solids in the skeleton and in the meat of the body; in the fresh stage we know only their weight taken together. I have assumed the percentage water-content of the freshly separated bones to be the same as that of the entire skeletal system. These values are sufficiently correct to give a clear picture of the differences in the relative proportions. I did not endeavor in these experiments to determine the composition of the whole body, but tried simply to illustrate the most striking differences.

In the determination of total solids, ash, and nitrogen (Kjeldahl) the usual methods were employed; in that of fat I used the method described of Baur & Barschall.[12] This procedure, which consists in the destruction of the nonfatty material by sulphuric acid and the extraction of the fat by shaking the solution so obtained two or three times with ether, is short and simple and gives as satisfactory results as the Soxhlet method. It is especially applicable in the Tropics, because during the greater part of the year the tap-water is so warm that it becomes necessary to use ice-water in the condensers to avoid losing too much ether.

Experiment No. 1.—Four dogs of one litter were used in experiment one. These were about two months old and all very much alike in appearance. In the beginning I had intended to study the influence both of different quantities and of different kinds of food upon growth and so gave meat only to two animals, and carbohydrates as well as meat to the other two.

Two of the four dogs were fed so that their weight increased rapidly (I and IV, Table 14), two were poorly nourished (II and III, Table 14). This experiment did not progress smoothly. The composition of the food was changed several times. From the sixteenth to the twentieth day, animals I, II, and III suffered from diarrhœa from some unknown cause. From this period until the fifty-sixth day no accident occurred. On the fifty-sixth day the native laboratory servant, who had been instructed to clean the stable with dilute carbolic acid solution, sprinkled pure phenol not only on the floor, but also on the dogs, and burned numbers I, II, and III so severely that they were promptly killed with ether to end their suffering. Number I escaped with only slight injuries. He was kept until the 8th of April, when he developed cramps and died in a few hours, apparently from internal injuries received from a fall.

During the relatively short period of this experiment animals I and IV increased in weight from about 1,400 to more than 3,000 grams.

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[12] *Arb. a. d. kais. Gesndhtsmte.* (1909), **30**, 55–62.

It is worth mentioning that number IV, receiving about 10 per cent less in calories than number I, very soon dropped somewhat behind the latter in weight.

EXPERIMENT I.—*Dogs I to IV.*

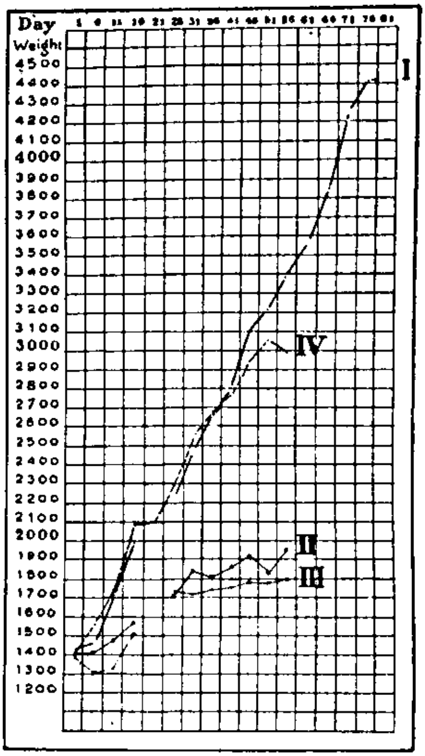

CHART 1.—Variations in weights of dogs I to IV of Experiment I.

Dogs II and III, which received practically the same amount of calories, increased but slightly in weight during the first forty days (from about 1,400 to 1,900 grams). The constancy in weight desired was reached between the fortieth and fiftieth day.

During the period of the experiment the appearance of the four animals changed considerably. While numbers I and IV were apparently well nourished and well proportioned, numbers II and III, although increasing in weight, began to appear emaciated. Their legs seemed to be unusually long and slender, while their heads appeared to be a trifle large in proportion to their bodies. I took a few measurements, which may illustrate this condition.

Dimensions of dogs on the fiftieth day of Experiment I.

No.	Entire length.	Circumference of chest.	Length of fore leg.	Length of hind leg.	Circumference of head.
	Cm.	*Cm.*	*Cm.*	*Cm.*	*Cm.*
II	45.0	30.0	25.6	31.2	20.5
III	43.5	27.5	24.8	30.3	20.3
I	51.0	33.0	28.0	33.0	20.6
IV	52.3	35.0	29.0	(?)	21.0

The term "live weight" in this paper is used to designate the weight of the entire animal before death. Those parts of the animal left after removing skin, internal organs, the digestive tract, and blood when it is bled to death, are called the "body." The "body" therefore consists of muscles, skeleton, nervous system, etc.

Analyses of the four animals used in Experiment I gave the following results:

TABLE 1, EXPERIMENT I.—*Composition of dogs I to IV.*

	Dog number—			
	II.	III.	IV.	I.
	Grams.	*Grams.*	*Grams.*	*Grams.*
Live weight	1,942	1,747	2,850	4,600
Body (muscles, skeleton, etc.)	1,206	1,133	1,986	3,040
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*
Per cent of live weight	62.1	64.8	69.7	66.1

TABLE 2, EXPERIMENT I.—*Weight of skin and organs of dogs II to IV.*

	Fresh.			Dry.		
	Dog II.	Dog III.	Dog IV.	Dog II.	Dog III.	Dog IV.
	Grams.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*
Skin	282.6	238	333	104	89	120
Brain	60.30	57.10	59.86	10.62	10.67	11.12
Liver	95.25	85.55	140.07	22.09	21.30	35.33
Lungs	42.26	41.20	67.25	7.56	7.36	10.79
Heart	20.20	17.83	24.39	3.73	4.04	5.41
Kidneys and spleen	36.20	32.40	45.37	6.30	6.10	9.83
Internal organs, total	193.91	176.98	277.08	39.68	38.83	61.46
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*
Per cent of live weight	10.00	10.10	9.70	2.04	2.22	2.15

TABLE 3, EXPERIMENT I.—*Weight of skin in per cent of live weight of dogs II to IV.*

Dog number—	Fresh.	Dry.
	Per cent.	*Per cent.*
II	13.6	5.35
III	14.6	5.09
IV	12.0	4.21

TABLE 4, EXPERIMENT I.—*Composition of bodies of dogs I to IV.*

	Dog number—											
	II.			III.			IV.			I.		
	Weight.	Per cent of—		Weight.	Per cent of—		Weight.	Per cent of—		Weight.	Per cent of—	
		Body weight.	Live weight.		Body weight.	Live weight.		Body weight.	Live weight.		Body weight.	Live weight.
	Grams.			*Grams.*			*Grams.*			*Grams.*		
Fat	30.7	2.5	1.6	21.8	1.9	1.8	107.8	5.4	3.8	309.9	10.2	6.7
Protein of muscles	167.0	13.9	8.6	168.0	14.9	9.6	289.0	14.5	10.2	382.5	12.6	8.0
Protein of bones	47.8	3.9	2.46	42.2	3.7	2.42	49.5	2.5	1.74	105.5	3.5	2.29
Ash of bones	68.3	5.7	3.52	61.5	5.4	8.52	64.9	3.8	2.28	96.4	3.2	2.10
Rest=(water, ash of muscles, etc.)	882.2	74.0	45.4	839.5	74.1	48.1	1,474.7	74.3	51.7	2,145.7	70.5	46.7

Experiment No. II.—Two dogs of strikingly similar appearance from the same litter were used for the second experiment, which began on January 21, 1909. Number V weighed 2,200 grams; VI, 2,750 grams. The mother of the dogs was a large animal. Both animals passed through a preparatory period of three weeks during which, by giving different quantities of food, they were brought to nearly the same weight.

Changes in weights of dogs V and VI (preparatory period).

Date.	Dog V.	Dog VI.
	Grams.	*Grams.*
January 21	2,200	2,750
February 1	2,600	2,800
February 10	3,100	3,200
February 18	3,300	3,250

Number V, of smaller weight in the beginning, was selected to be so fed as to permit a normal growth; number VI, the heavier animal, was to be kept at a constant weight.

Only one accident occurred during the entire course of the experiment. (Table 15.) From the fourteenth to eighteenth day, number V suffered from overfeeding. By a slight restriction of food for two days, the trouble was remedied, but no increase in weight occurred from the eleventh to twenty-first day.

Experiment II.—*Dogs V and VI.*

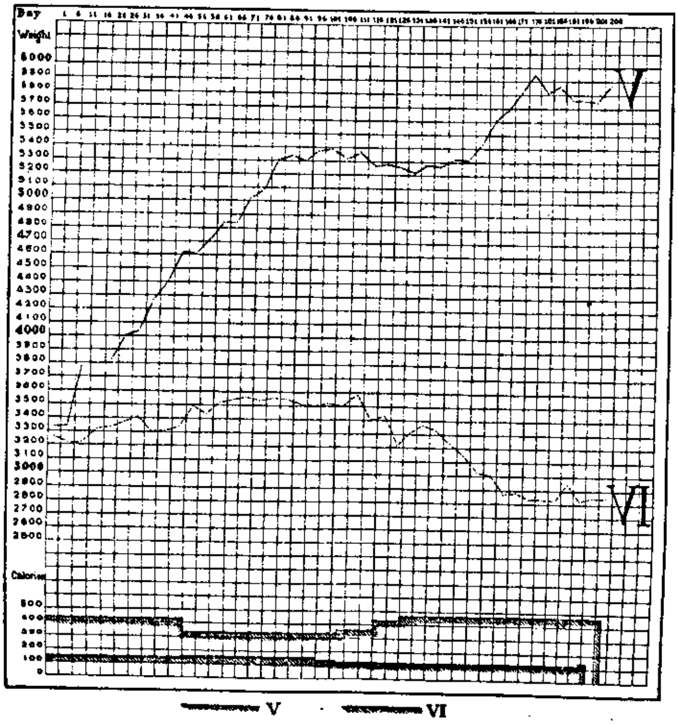

Chart 2.—Variations in weights of and amounts of food taken by dogs V and VI of Experiment II.

Number V, in the first fifty days, was given three times as much food as number VI, the latter receiving 140 calories only (meat 10 parts and starch 1 part). The body weight of number VI increased about 200 grams, while number V gained 1,300 grams. In the next fifty days, number V was given only 335 calories and the increase in weight was 750 grams. Number VI received a very slight increase (150 calories) because of its greater body weight, and gained about 100 grams.

The composition of the food was now changed, a mixture of 1 part of starch and 2.5 parts meat being supplied. The proportion of protein in the food seemed to me sufficient, about one-third of the total caloric intake being furnished by protein. Number V, when receiving as much as 480 calories, increased only slightly in weight; the animal now had reached almost the stage of adult life, and the greater part of the increase in weight was due to storage of fat and not to growth. The intake of number VI was at first reduced to 135 calories. Owing to the fact that the animal's weight still seemed to increase, I further reduced the food to about 120 calories, which amount, I thought, would furnish sufficient energy to keep the body weight constant. However, on this diet the animal, instead of gaining weight, lost, especially toward the last.

The changes in appearance which the two dogs showed during the course of the experiment are of great interest. Number V increased in weight and size just as any other normal dog would and was a fine looking, well nourished animal. Number VI resembled dogs numbered II and III of the first experiment, but the changes from the normal were more pronounced. Although increasing slightly in weight, the animal from day to day became thinner, but taller and longer. We see here the paradox of an animal becoming emaciated while gaining in weight. In the end, number VI seemed to be only skin and bones. Nevertheless, the dog was quite lively, jumping around and performing a really astonishing amount of muscular work.

On the one hundred and seventy-fifth day of the experiment a photograph of both dogs (Plate I) was taken, showing their general appearance and relative size, the distance from the lens of the camera being the same for both. The most surprising fact is that number VI, while weighing only two-fifths as much as number V, seemed to be not very much smaller. Indeed, the animal had grown all the time so far as length of body and size of extremities were concerned.

The following measurements taken on the one hundred and eighty-third day show that there is only a slight difference in length between the two dogs, while the circumference of number VI is considerably less than that of number V.

Measurements of dogs V and VI on the one hundred and eighty-third day.

	Dog number	
	V.	VI.
	Cm.	*Cm.*
Nose to os occipitale	15.5	15.0
Nose to tip of tail	53.0	49.0
Length of fore leg	35.0	34.0
Length of hind leg	38.5	37.5
Circumference of head	26.5	25.5
Distance from ear to ear	8.4	7.5
Circumference of chest	37.5	30.0

From the one hundred and ninetieth to the one hundred and ninety-fifth day of the experiment, number VI no longer exhibited such liveliness and muscular strength, but appeared to be lazy and weak. Therefore, on the two hundredth day, it seemed necessary to increase the amount of his food. At first, 150 calories were given, but the animal was apparently already too weak to recover, for it died on the morning of the two hundred and third day, doubtless of general weakness. No sign of disease was shown at autopsy except extreme emaciation, an absolute lack of subcutaneous fat, general anæmia of all the organs, and an unusually soft consistency of the muscles.

Number V was killed as a control animal a few days later by bleeding. The animal showed a well-developed layer of subcutaneous and visceral fat and normal internal organs.

The analyses gave the following results.

TABLE 5, EXPERIMENT II.—*Composition of dogs V and VI.*

	Dog V (5,885 grams).		Dog VI (2,708 grams).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	Grams.		*Grams.*	
Brain	[a]52	0.90	[b]58	2.00
Liver	153	2.60	97	3.62
Heart	39	0.66	17	0.61
Lungs	60	1.01	29	1.07
Spleen	12	0.21	2	0.01
Kidneys	35	0.60	22	0.81
Digestive tract empty	387	6.58	155	6.00
Other internal organs	236	----------	52	----------
Body (muscles, bones, etc.)	3,835	65.2	1,624	60.0
Skin	662	11.2	339	12.5
Blood	[c]346	----------	[d]40	----------
Content of stomach and intestines by difference	168	----------	273	----------

[a] Dry 12.8 grams.

[b] Dry 11.2 grams.

[c] Killed by bleeding.

[d] Died; blood collected from large vessels after death.

TABLE 6, EXPERIMENT II.—*Weight of certain of the bones of dogs V and VI.*

	Dog V.		Dog VI.	
	Fresh.	Dry.	Fresh.	Dry.
	Grams.	*Grams.*	*Grams.*	*Grams.*
Femur	28.35	16.53	27.2	9.85
Tibia-fibulare	25.00	15.14	23.2	9.77
Scapula	13.55	6.68	11.4	5.05
Humerus	27.45	15.63	26.8	9.84
Radius	11.65	7.36	11.05	4.84
Ulna	10.30	6.54	10.9	4.85
3 ribs (5, 6, 7)	10.70	5.02	8.75	3.48
Total	127.00	72.80	119.3	47.68
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Per cent of live weight	2.16	1.24	4.41	1.76

TABLE 7, EXPERIMENT II.—*Percentage composition of dogs V and VI.*

	Dog V.			Dog VI.		
	Weight.	Per cent of—		Weight.	Per cent of—	
		Body weight.	Live weight.		Body weight.	Live weight.
	Grams.			*Grams.*		
Fat	271.5	7.1	4.6	7.7	0.5	0.3
Protein of muscles	632.3	16.5	10.7	147.6	9.0	5.4
Protein of bones	138.6	3.6	2.4	110.1	6.8	4.0
Ash of bones	131.0	3.4	2.2	126.3	7.8	4.7
Remainder of body, (muscles, ash, etc.)	2,661.6	69.4	45.2	1,232.3	75.9	45.5
Fat in organs	137.7		2.3	5.0		0.2
Protein in organs	120.6		2.0	51.1		1.9
Total fat	409.2		6.9	12.7		0.5
Total protein	891.5		15.1	308.8		11.3

TABLE 8, EXPERIMENT II.—*Composition of bones of dogs V and VI.*

	In the fresh bones.		In the solids.	
	Dog V.	Dog VI.	Dog V.	Dog VI.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Water	42.76	60.02		
Protein	22.06	18.05	38.54	45.15
Ash	20.79	20.70	36.32	51.78
Fat	12.34	0.09	21.55	0.23

TABLE 9, EXPERIMENT II.—*Water and solids in different parts of the body.*

	Dog V.		Dog VI.	
	Total solids.	Water.	Total solids.	Water.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Blood	[a]18.84	81.16	[a]5.10	94.90
Brain	24.60	75.40	19.31	80.69
Bones	57.24	42.76	39.98	60.02
Muscles	29.12	61.88	15.24	84.76

[a] Protein = N×6¼.

Experiment No. III.—For the third experiment seven dogs were taken originally. Number VIII matched number IX, and number X matched number XI extremely well, while numbers VII, XII, and XIV were comparable fairly well.

EXPERIMENT III.—*Dogs VIII, XI, XII, XIV.*

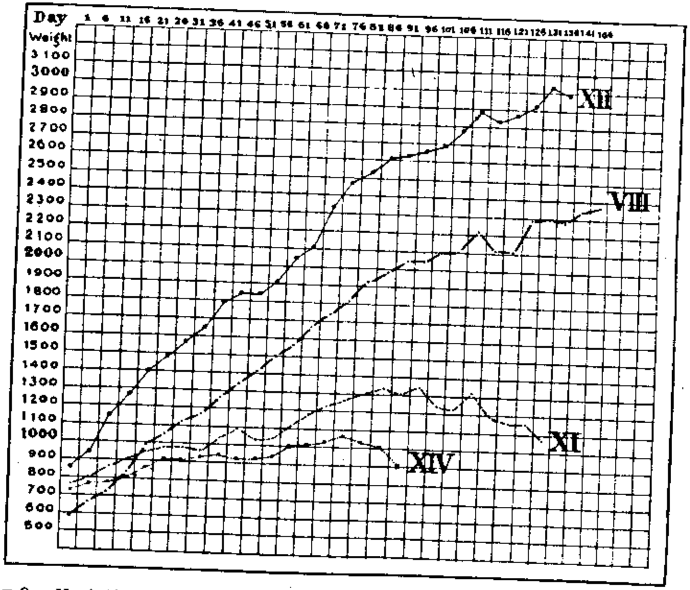

CHART 3.—Variations in weights of dogs VIII, XI, XII, and XIV of Experiment III.

Dogs numbers VII, IX, and X were killed on the eighteenth day of the experiment through the same accident by which animals I, II, and III were lost. Only four dogs were left, these being comparable more by reason of age and weight than by descent. In spite of the unfortunate accident, this experiment was continued for some time. (Table 16.) It was planned to keep the weights of dogs numbers XI and XIV constant. For twenty days each animal received 110 calories and their weights increased from 760 to 950, and from 732 to 866 grams, respectively. Number XIV was given about 75 calories. On this diet its weight remained practically stationary. The animal became thinner and weaker from day to day and died from emaciation and weakness on the ninty-first day of the experiment. The body was not analyzed chemically because it was thought at the time that the composition of the starved animal would be of no special interest.

Number XI after the first twenty days received 90 calories, then 95, and finally 100 calories, and its body weight increased from about 950 to 1,150 grams. This dog presented the same picture as number VI of the first experiment, for it became thinner and taller during the entire period. It was killed on the one hundred and thirty-sixth day and analyzed. (Tables 10 and 11.)

Dog number VIII, the lightest at the beginning of the experiment, was given an ample supply of food and during one hundred and forty-five days increased from 600 to 2,350 grams. Dog number XII, weighing 850 grams at the beginning, received the equivalent of but a few more calories, but its weight nearly reached 3,000 grams in one hundred and forty days. Both animals were analyzed and a study of table number 11 reveals the interesting fact that dog number VIII had a much greater tendency to put on fat, while the muscles of number XIII increased markedly in weight. This is explained by the fact that number VIII was of a smaller breed than number XII.

TABLE 10, EXPERIMENTT III.—*Composition of dogs VIII, XI, and XII.*

	Dog XI (1,100 grams live weight).		Dog VIII (2,375 grams live weight).		Dog XII (3,000 grams live weight).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	Grams.		*Grams.*		*Grams.*	
Liver	48		88		78	
Heart	10		21		21	
Lungs	11		19		26	
Spleen	2		5		7	
Kidneys	24		27		24	
Digestive tract	102		159		223	
Remaining internal organs	45		89		85	
Total internal organs	242	22.0	408	17.2	465	15.5
Brain	49	4.5	48	2.0	57	2.9
Body	645	58.6	1,413	59.5	1,946	64.8
Skin	134	12.2	309	13.0	294	9.8
Blood	66	6.0	138	5.9	197	6.6
Content of stomach and intestines by difference	23		107		198	

TABLE 11.—*Fat and protein in organs and muscles of dogs VIII, XI, XII.*

	Dog VIII (2,375 grams live weight).		Dog XII (3,000 grams live weight).		Dog XI (1,100 grams live weight).	
	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.	Weight.	Per cent of live weight.
	Grams.		*Grams.*		*Grams.*	
Fat in muscles	51.9	2.2	30.1	1.0	7.0	0.6
Fat in organs	21.6	0.9	19.9	0.7	4.3	0.4
Total fat	73.5	3.1	50.0	1.7	11.3	1.0
Protein in muscles	155.9	6.6	229.4	7.6	54.0	4.9
Protein in organs	61.0	2.6	78.6	2.6	31.9	2.9
Total protein	216.9	9.2	308.0	10.2	86.1	7.8

Experiment No. IV.—Experiment number IV was the most successful one. Four dogs (A, B, C, D) of the same litter, about 5 weeks old, were treated with thymol early in July, 1909, and prepared for the experiment. The animals were as nearly alike as could be desired in size and general appearance. The experiment began August 1, 1909. On the fortieth day the four dogs were of nearly the same weight and were photographed. On the forty-fifth day, dog D was killed and analyzed for comparison. (See Table 13.) Dog B was allowed to grow as rapidly as possible; dog C was not given as abundant a supply of food as B, and dog A was fed only a sufficient amount to keep his body weight constant.

The mineral constituents of the food were disregarded in the experiments described above. If a young, rapidly growing dog is fed a diet of meat and starch such as was used in these experiments, it very probably will receive an insufficient supply of calcium salts. In order to remove this possible source of error there were added to the daily food of each dog from 1.0 to 1.5 grams of calcium phosphate in addition to the sodium chloride.

The experiment progressed smoothly so far as dogs A and B were concerned (see Table 17), but on the one hundred and twenty-second day dog C was taken ill suddenly and died in about twenty hours. The cause of death could not be determined at autopsy; it may have been distemper.

Dog B, which received from 400 to 680 calories daily, increased in weight from 1,500 grams (2,000 on the fortieth day) to about 7,400 grams on the five hundredth day.

Dog A was not kept on quite so low a diet as the other animals (VI, XI, and XIV), the body weights of which were to remain constant; at first it received 110, then 130, and, finally, from the one hundredth day, 175 calories per day. Its body weight increased so little that it could be regarded as practically constant.

EXPERIMENT IV.—*Dogs A to D.*

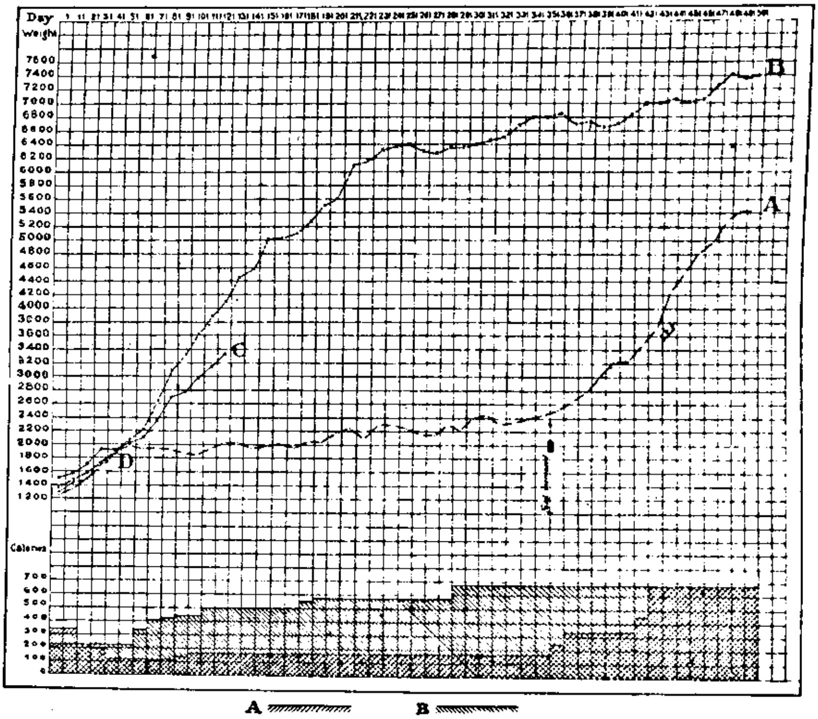

CHART 4.—Variations in weights of and amounts of food taken by dogs A to D of Experiment IV.

The animal in every respect presented the same type of development as number VI. It gradually became thinner, taller, and longer to the two hundredth day, when it no longer changed in appearance. The animal consisted mainly of skin and bones, but it still had enough muscle to enable it to move with vivacity, in fact it was more active than dog B, although the latter was three times as heavy. A photograph of both dogs was taken on February 15, the one hundred and ninety-ninth day. This, better than any description, shows the difference in size and appearance of the two animals. (See Plate II.)

The dogs were kept for about one hundred and fifty days longer. Dog A continued to receive the same diet. The diet of B was increased to 680 calories per day. The body weight of dog A remained practically constant and the dog did not change appreciably in general appearance.

Dog B, with a more than ample diet, became somewhat larger and much fatter, and increased in weight from about 5,500 to 7,000 grams.

The experiment was continued in this way to the three hundred and fiftieth day, when another photograph (Plate II) was taken. At the same time the animals were measured. (See Table 12.) On comparing the photographs of the dogs taken on the two hundredth and the three hundred and fiftieth day, it is apparent that during these last five months dog A had not only kept its body weight constant, but also had not grown.

Both animals were more than one and one-fourth years old at this time, and had reached the age at which dogs usually cease to grow. This is proved by the fact that dog B in spite of its ample diet showed no further increase in size and only very little in weight.

If the animals (A and B) had been killed at this time the increase or decrease in weight of the different organs and parts of the body since the forty-fifth day, as compared with the body of the control dog D, could have been determined exactly. We would then have had further evidence bearing upon the question as to which organs or parts of the body increase at the expense of others. However, I considered that I had already accumulated sufficient data on this point. These animals had now become invaluable for the solution of another and biological problem, namely, whether dog A, if it were now to be given an abundance of food, would increase in weight and size and make good the growth it lost in its youth. It also was necessary to determine whether dog A would finally attain the same weight and size as dog D.

Therefore, starting on the three hundred and fifty-fifth day, the food of number A was augmented to 230, 280, 340, 450, and finally 680 calories each day. An increase in body weight was noticed almost at once and the animal continued to gain steadily. At the same time it became rounder, the bones did not show through the skin as they did before, and the sharp angles disappeared. The diet from the four hundred and thirty-first day was the same as that of the control dog B, and following this a further increase in weight was observed. The animal continued to fatten, but apparently it did not increase in length nor in height. In order to determine if this dog still had the capacity for growing, to offset the lack of growth brought about by his restricted diet in youth, the same measurements were taken on the five hundredth as were recorded on the three hundred and fiftieth day, before the food was increased. These values are given in the following table and indicate clearly that during this period dog A, while receiving a more than ample diet and gaining in weight from 2,450 to 5,440 grams, practically did not increase in length or height, but only very greatly in circumference.

Table 12.—*Weights and measurements of dogs A and B.*

	Dog A.		Dog B.	
	355th day.	500th day.	355th day.	500th day.
Weight in grams	2,450	5,440	6,850	7,400
	Cm.	*Cm.*	*Cm.*	*Cm.*
Length from nose to atlas	16.0	16.0	18.0	18.2
Length from nose to os coccygis	54.0	55.5	66.0	66.0
Length from nose to end of tail	71.0	74.0	88.0	89.0
Distance from ear to ear	8.0	9.4	11.4	11.5
Circumference of head	23.5	26.5	28.5	29.0
Circumference of neck	15.5	23.0	27.0	28.0
Circumference of chest	28.0	39.5	43.0	47.0
Circumference of abdomen	21.0	34.0	33.0	37.0
Length of fore leg	25.0	26.0	34.0	34.5
Length of hind leg	31.0	31.0	37.5	37.5
Height from ground	29.5	31.5	35.5	36.0

On the five hundredth day, as compared with the three hundred and fiftieth, the aspect of dog A had changed entirely. The slender, emaciated animal had become an overfattened but dwarfed dog. Photographs of both A and B were taken on the five hundred and first day. (See Plates III and IV.) It is apparent that dog A, in spite of the ample diet given during the last five months, had lost the "tendency to grow." However, because of the ample food which had been given to it, it was able to store up fat, thus increasing in weight and thickness, but not in size.

It having been proved that dog A had lost its normal capability of growing, it was decided to finish the experiment by killing and analyzing both animals. This was done on the five hundred and fifth and five hundred and sixth day for A and B, respectively. The autopsies showed no remarkable features, except a great amount of fat in dog A, the subcutaneous layer as well as the muscular and mesenteric fat being considerably greater in amount than that of its normal brother B. The weights of the organs and the bones, selected as usual, were determined. (Table 13.)

TABLE 13, EXPERIMENT IV.—*Composition of dogs A to D.*

	Dog D (killed Sept. 18, 1909).	Dog C (died Dec. 3, 1909).	Dog A (killed Dec. 20, 1910).	Dog B (killed Dec. 21, 1910).
	Grams.	*Grams.*	*Grams.*	*Grams.*
Live weight	1,985	3,410	5,474	7,178
Liver	62	----------	152	171
Heart	13	----------	38	59
Lungs	20	----------	58	87
Spleen	5	----------	12	17
Kidneys	18	----------	32	59
Digestive tract empty	125	----------	250	316
Remainder of internal organs	79	----------	167	227
Total weight of organs	322	----------	709	936
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Organs in per cent of live weight	16.2	----------	12.9	13.0
	Grams.	*Grams.*	*Grams.*	*Grams.*
Blood collected	95	----------	263	418
Skin	320	601	808	869
Brain	52	60	56	65
Remainder of body=(muscles, bones, etc.)	1,164	----------	3,637	4,816
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Body in per cent of live weight	58.6	----------	66.4	67.0
	Grams.		*Grams.*	*Grams.*
Content of intestines by difference	84	----------	57	141
Weight of:	*Grams.*	*Grams.*	*Grams.*	*Grams.*
Femur	11.0	17.3	16.23	24.74
Tibia-fibulare	8.6	15.1	12.89	20.63
Scapula	5.0	8.8	7.10	13.61
Humerus	10.0	16.85	15.45	22.84
Radius	4.05	7.75	5.92	9.16
Ulna	3.75	7.1	5.72	8.59
Three ribs (5, 6, 7)	4.25	8.8	5.78	9.90
Total weight of nine bones	47.00	81.6	69.09	109.47
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
Total of nine bones in per cent of live weight	2.37	2.39	1.26	1.53

Both animals had been given an excess of food to enable them to grow to the greatest possible extent and therefore the relative amounts of fat and flesh, as compared with the skeletons, were larger than in the case of the control dogs C and D which had been killed more than a year before; the bones in both animals were relatively lighter. However, it will be seen that the bones of dog A, in which the growth was suppressed in the first period of the experiment, weighed considerably less in proportion to the total live weight than was the case with the normal control animal B, this being the result of the excessive feeding of A. Plate IV shows several bones of both A and B, and demonstrates that the various bones of A had not reached the dimensions of those of its normal brother, in spite of the fact that for five months it had been given a more than ample diet.

DISCUSSION OF EXPERIMENTS.

INFLUENCE OF A RESTRICTED DIET ON THE WEIGHT AND APPEARANCE OF GROWING DOGS.

In six animals (II, III, VI, XI, XIV, A) an attempt was made to suppress growth by restriction of food. All these animals were far behind their normal brothers (I, IV, V, VIII, XII; B and C, respectively) in weight. In spite of the restricted diet there was a slight increase in weight in the first group. The weight of dog number VI of the second set increased but very slightly in the first period, after that it remained constant, and decreased only at the end of the experiment. Number XI of the third set also lost but very little; the weight of number XIV remained practically constant. The weight of dog A of the fourth group remained nearly the same for ten months (fortieth to three hundred and fiftieth day), increasing but very slightly. The weight in all these dogs was so nearly constant that we are justified in so regarding it, the increase or decrease amounting to a few grams only. Did a cessation of growth take place with this constancy in weight? By no means! We have already seen that in spite of the constancy of weight all the dogs increased in length and height. At the same time the animals became leaner, fat and muscles diminished, the well-rounded form of the body disappeared, and the bones became visible in outline directly under the skin. The dogs when in this condition were by no means weak. They jumped about and were often more active than their normal brothers, but the latter had to carry nearly three times as much live weight.

This stage, in which the dogs grew leaner but longer and taller, while the weight was practically constant, lasted for from three to five months, varying somewhat with the degree of restriction of the food. If now the restricted diet was continued, when the animals were emaciated to an extreme degree, they died of inanition following a slight loss of weight, but if the food was increased slightly, it was possible to keep the emaciated animal at a constant weight.

From the two hundredth until the three hundred and fiftieth day—that is, for five months—dog A was kept at a constant weight and there was no noticeable change in its size nor in its appearance; in fact this constancy indicated a cessation of growth. Therefore we must conclude that it is possible by a suitable restriction of diet to maintain young, growing dogs at a constant weight for considerable lengths of time. While the weight remains constant, important changes occur in the animal's body. These consist in a continuous increase in the length and height of the dog, combined with a more or less extreme emaciation.

Apparently, in spite of the constancy of weight, the skeleton grows and increases both in size and mass. If this be true, other parts of the body must have lost in mass. In all probability not only the relative masses of the different parts of the body, but also the quantities of the various body constituents, have changed considerably. Information concerning these alterations is furnished by the analyses of the bodies of the animals.

RELATIVE AMOUNT OF CHANGE IN CERTAIN PARTS OF THE BODY AS COMPARED WITH OTHER PARTS.

The skeletal system shows the most striking difference in general composition. The quantities of protein and ash in the bones of the three dogs, IV, II, and III, are nearly the same in spite of the differences in weight, number IV, 2,850 grams; number II, 1,940 grams; and number III, 1,750 grams. The weight of the bones (ash and protein) in relation to the live weight is considerably higher in dogs number II and III (9.6 per cent and 9.1 per cent) than in dog number IV[13] (5.8 per cent).

We find even more pronounced differences in comparing the compositions of dogs V and VI. Several corresponding bones of these two animals were isolated and analyzed. The weight of each bone of dog number VI was not much less than was the corresponding bone of dog number V, although the body weight of the former was 5,885 grams and of the latter 2,710 grams. The total weight of the nine bones selected from the normal dog, number V, was 127.0 grams or 2.16 per cent of the live weight; the bones from the dog of constant weight, number VI, weighed 119.4 grams or 4.41 per cent of the live weight.

In experiment IV, I isolated the corresponding bones from two other young dogs of the same litter, at a time when they were of different weights and different ages. These animals (C and D) were of equal weight at the time D was killed and analyzed. Dog C was then fed normally for about seventy-five days and analyzed. These results show:

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[13] The bones of dog number IV contain proportionally more protein and less ash than those of numbers II and III. This fact is still more pronounced in dog number I. These animals were fed on a diet poor in calcium (meat and starch without addition of lime) and the changes in the skeletal system correspond to those described by me as occurring as a consequence of such a diet.

Live weight and weight of nine bones, dogs D, C, and V.

Dog.	Live weight.	Weight of 9 corresponding bones.	Per cent of live weight.
	Grams.	*Grams.*	
D	1,985	47.0	2.37
C	3,410	81.6	2.39
V	5,885	127.0	2.16

The weights of the corresponding bones expressed as percentages of the respective live weights are nearly the same in dogs D, C, and V. We may assume that in dog VI, which was kept at constant weight, these bones amounted to about 2.2 per cent of its live weight before the experiment began. Hence, on or about the first day of the experiment, when the animal weighed 3,200 grams, these nine bones had a weight of about 70 grams. After about two hundred days, the same animal weighed 2,800 grams only, and the bones had increased in weight to 119 grams.

The composition of a normal dog is approximately constant (Voit,[14] Pfeiffer,[15] Stockhausen [16]), the skeleton 15 per cent, the muscles (flesh) 50 per cent of the live weight. The skeleton plus flesh of our normal dog V was found to equal 65.2 per cent of the live weight, which is in very close agreement with these figures. We are justified in regarding 15.0 per cent as skeleton, 50.2 per cent as flesh, 65.2 per cent skeleton and flesh.

The entire skeleton therefore would weigh 883 grams. Now, if we know that the same fraction of fresh bones, which in dog V weighed 127 grams, was 119.4 grams in dog VI, we can apply the results obtained with the nine bones to the entire skeleton, as follows:

$$\frac{883 \times 119.4}{127} = 830 \text{ grams.}$$

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[14] *Ztschr. f. Biol.* (1894), **30**, 510–522.

[15] *Ibid.* (1887), **23**, 340–380.

[16] *Biochem. Ztschr.* (1909), **22**, 244.

In the beginning of the experiment the skeleton weighed 15 per cent of 3,200 grams = 480 grams. From this figure the following values are obtained for the increase of the skeleton:

	Live weight.	Skeleton.
	Grams.	*Grams.*
Beginning of experiment	3,200	480
End of experiment	2,800	818
Increase		338

Both these experiments (I and II) show conclusively that, *if a growing dog is kept at a constant weight, or even at a slightly decreasing weight, the bones continue to increase in weight and therefore to grow, although not quite so rapidly as in a normally fed control animal.* If the bones have absolutely and relatively increased in weight, while the total weight of the animal has been kept constant, it is obvious that other parts of the body must have lost in weight.

The organs are apparently not involved in this process of consumption. In the first experiment the weight of lungs, liver, heart, spleen, and kidneys only was taken; all these organs had their normal blood content, the animals not being killed by bleeding as was the case later. The total weight of these organs amounted to 10.0 per cent and 10.1 per cent, respectively, of the live weight of the two dogs which were on a low diet, as compared with 9.7 per cent in the normal one. In experiments II, III, and IV the weight of all the organs of the thorax and abdomen was determined, the intestinal tract having been cleaned previously. The results are summarized in the following table:

Number of dog.	Live weight.	Total weight of organs.	Per cent of live weight.
	Grams.	*Grams.*	
V (N)[a]	5,885	822	14.0
VI (C)[a]	2,710	374	13.7
XII (N)	3,000	465	15.5
VIII (N)	2,375	408	17.2
XI (C)	1,100	242	22.0
D (N)	1,985	322	16.3

[a] (N) The dog grew under normal conditions. (C) The dog was kept at a constant weight.

The values vary somewhat, but there is no indication that the organs of the animals kept on a lower diet lost in weight. On the contrary, the percentage weight of the organs of number XI is slightly higher than that of the control dogs of the same age, but of more or less normal live weight.

In experiment I the proportion of total solids in the organs was also determined. As Table 2 shows, there is practically no difference in the amount of dry organs, expressed in percentage of live weight, for the three different dogs.

There is little to be said about the behavior of the different organs. It appears in general that those of the digestive tract (liver, kidneys, and intestines) have increased somewhat, while the others, such as the spleen, heart, and lungs, have suffered a slight loss.

The brain deserves special consideration. In experiment I the weights of the brains of the three dogs did not differ in the same way as those of the other organs. Their weights were nearly identical, in spite of the difference in body weight of the animals. The same holds true for experiment III. In experiment II the dog of smaller body weight (VI) had a heavier brain than the normally developed animal (V). However, Table 9 shows that the absolute amount of solids in both brains is nearly the same, being slightly smaller in that of dog VI than in that of dog V.

Live weight and brain weight in eight dogs.

Number of dog.	Live weight.	Weight of brain.
	Grams.	*Grams.*
II (C)[a]	1,940	60.3
III (C)	1,750	50.1
IV (N)[a]	2,850	59.9
V (N)	5,885	52.0
VI (C)	2,710	58.0
XI (C)	1,100	49.0
XII (N)	2,375	48.0
VIII (N)	3,000	57.0

[a] (N) Grew under normal conditions. (C) Kept at a constant weight.

The figures in the foregoing table show conclusively that the brain has nearly the same weight in a dog kept at a constant weight as in a normally developed animal.

The weight of the brain in relation to the body weight in a younger animal is higher than in an older one, and the brain does not grow in the same proportion as do the other organs. This is well illustrated by the following data, taken from those recorded for the two dogs of experiment IV, one of which (D) was killed seventy-five days before the other (C). While the live weight had increased from about 2,000 to 3,400 grams, the weights of the brains at the two different periods are 52 and 60 grams, respectively; i. e., there was 70 per cent increase in the live weight, and only 15 per cent increase in brain weight.

According to data taken from Monti[17] the brain of a child increases in weight from three to four times, while the weights of other organs increase about ten times.

The skin shows a slightly higher percentage of the body weight in those animals kept at a constant weight than in the normal, control dogs.

	Dog.	Weight of skin in per cent of body weight.	
		Fresh.	Dry.
Experiment I	II (C)[a]	13.6	5.35
	III (C)	14.6	5.09
	IV (N)[a]	12.0	4.21
Experiment II	V (N)	11.2	
	VI (C)	12.5	
Experiment III	XI (C)	12.2	
	VIII (N)	13.0	

[a] (N) Grew under normal conditions. (C) Kept at a constant weight.

These figures indicate that, while the weight was constant, the skin increased very slightly in weight.

Only the flesh, muscles, and fat of the body remain as the tissues which must have lost during the course of the experiments. The degree of this loss of flesh will be best recognized by considering the chemical composition of the different animals.

CHANGES IN THE CHEMICAL CONSTITUTION OF THE BODY.

The quantities of the different constituents are reduced to percentages of the live or body weight in order to facilitate this calculation. The absolute quantity of protein, fat, etc., is, of course, smaller in the dogs kept on a low diet than in the normally fed animals. This may not be absolutely correct in regard to the fat if the control animal was overfed during the course of the experiment. However, if the quantity of fat is far below the values which we find in the normal animals, there of dog number VI contained about one-fourth as much protein as that of dog V and of normal dogs (18 to 20 per cent).

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[17] Das Wachstum des Kindes in "Kinderheilkunde in Einzeldarstellungen" (1898), 555.

The muscles contained only one-half of the normal amount of total solids.[18] The water content of the brain had also increased considerably. It will be remembered that the weight of the fresh brain of dog VI was 57 grams as compared with 52 grams for that of the full-grown control dog V. However, the water content was so much greater that the amount of total solids in the brain of dog VI was in reality smaller than that of number V. This process of hydration (Verwässerung) brings about the condition in which the weight of the brain of a dog kept at low diet is greater than that of a normal control animal.

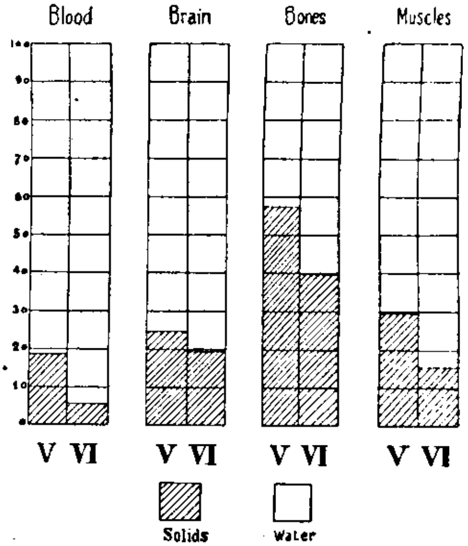

DIAGRAM 2.—Percentage of water and solids in blood, brain, bones and muscles of dogs V and VI of Experiment II.

The bones also show an increased water content in dog VI, as compared with dog V. However, in this case the percentage of ash in the bones is not diminished, and that of protein only very slightly so. Water in the starved bone really takes the place of fat in the normal one. These conditions are shown in diagram III.

The replacement of body substances by water in the different parts of the body, and the almost complete destruction of fat, demonstrates that all the animals on low diet were in a stage of starvation. Indeed, while their body weights remained constant, or were increased slightly, the animals were losing body substance, so that, while 1 gram of live weight of dog VI represented only 0.55 calories, the same weight of dog V represented 1.42 calories. This latter value agrees well with Rubner's findings (1 gram of dog equals 1.50 calories). Nearly two-thirds of the energy which dog number VI had stored at the time the experiment began must have been consumed during the experiment.

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[18] For this determination 25 grams of lean muscle from corresponding parts of the leg were selected, weighed and dried. The quantity of air-dried muscle was determined, then the dried material was powdered and the water content of this powder determined.

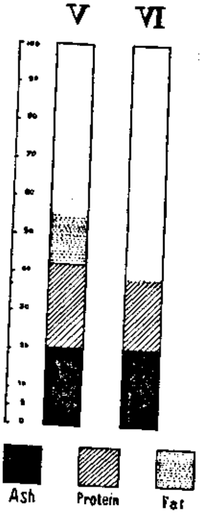

DIAGRAM 3.—Composition of bones of dogs V and VI of Experiment II.

It is quite interesting to compare the composition of the dogs which were kept on a low diet and the body weights of which remained constant or even increased slightly with that of adult animals which have undergone starvation.

During starvation of adult animals all parts of the body, even the skeleton, lose in mass. Skin, hair, and organs lose more than the muscles, but in our young dogs the muscles lose considerably more than the organs, which suffer scarcely any loss. Muscles, organs, brain, and spinal cord of a starved adult dog have the same water content as they have with normal dogs; the blood even becomes somewhat richer in solids. The converse is true with our dogs for there is a large decrease of solids, which is the most pronounced in the blood. However, in one respect the phenomenon is the same for starved young and for adult dogs, that is, the loss of fat from the muscles is comparatively greater than that from the organs.

ENERGY REQUIREMENT AND FOOD CONSUMPTION.

Because the animals kept at constant weight during the experiment lost energy normally belonging to their bodies, we may conclude that the energy given in the food was less than was required for maintenance alone.

The energy requirement for the maintenance of a growing animal is equal to that for an adult of the same size. According to the surface law, we can find the amount of energy required for maintenance for dogs of any weight by means of the following formula:

$$E = 1039 \times 11.3 \sqrt[3]{W^2}, \text{ where } E = \text{energy and } W = \text{weight.}$$

Rubner has shown that a dog of about 6 kilos requires for maintenance 50 to 55 calories per kilo of body weight, a value 10 per cent below that given by the above formula.

In order to make the conclusion clear it will be necessary to compare the energy requirements of those dogs the body weights of which remained constant with the total number of calories actually given to them in their food.

The two dogs in experiment I, receiving from 80 to 85 calories, kept their weight constant at from 1,800 to 1,850 grams. There can be no doubt that these animals received considerably less than the required amount of energy, which should be from 150 to 160 calories. In spite of this fact they not only did not lose in weight, but even showed a slight tendency to increase. However, this experiment was comparatively short and we do not know how the animals would have behaved later on the same food.

In experiment III one animal, number XIV, of less than 1,000 grams, received from 70 to 75 calories and increased slightly in weight. Its requirement, according to the surface law, was from 115 to 120 calories. This animal died in ninety days, probably of inanition.

Dog XI of about 1,000 grams increased its weight slightly but constantly, while receiving from 90 to 95 calories, the requirement being from 125 to 130 calories. This animal began to lose weight, beginning with about the ninetieth to the one hundredth day and continued to lose when the energy intake was increased to 100 calories.

In experiment II a dog (VI) of more than 3,250 grams body weight received 140 calories, about one-half only of its requirement (250 calories), and within fifty days increased nearly 250 grams. As 270 calories were required for maintenance at this period, the intake was increased to 150 calories; then the body weight approximately remained constant, but still had a tendency to rise. In the next part of the experiment 135 and soon thereafter only 120 calories were given. Following this, the body weight began to fall. The animal then died of inanition.

The body weight in the last experiment remained at a standstill for more than two hundred days in an animal of from 2,000 to 2,200 grams (dog A) which at first received 125, then 150, and later 170 calories, whereas 190 to 200 calories were required according to the surface law.

All these animals while receiving a considerably smaller quantity of energy than that required for maintenance, not only did not lose in body weight, but in the initial part of the experiment increased slightly.

The animals in the beginning of the experiment were well nourished with a fair storage of fat in their tissues. The growth of such an animal can not fully be stopped by restricting its food; for if we gave it the full-requirement for maintenance, certain parts of its body, especially the skeleton, would undoubtedly grow, thus increasing the weight of the animal. If we wish to keep such an animal from increasing in weight, we must starve it by giving so low a diet that the gain in weight, produced by the increase of certain parts of the body as an effect of their growth, is compensated by the loss in body substances used for maintenance in addition to the insufficient amount of calories taken in the food. The condition mentioned in the first lines of this paragraph is the one which we encounter in dogs II, III, XIV, XI, VI, and A at the beginning of the experiment. It is for this reason that we find such a great restriction of food necessary in order to prevent an increase in body weight, or to allow only a very slight one. In this period we are not able to suppress the growth by restricting the food, and constancy of weight does not indicate a cessation of growth.

However, these conditions change the longer the time during which this severe starvation lasts. If the greater part of the energy stored to give the reserve forces to the body is consumed, the animal, without losing in weight, becomes very much emaciated. If the low diet is continued, the animal finally loses somewhat in weight, and soon dies in a completely emaciated condition. This is simply because the animal does not have much more to lose. This explains the course of the experiments on dogs XIV and VI, in which case we could demonstrate plainly an entire loss of all reserve stuffs (fat) and a severe destruction of body proteins as well.

If instead of continuing the low diet, which initially was necessary to prevent an increase in weight, we follow it with sufficient food for maintenance or nearly that amount, the animal not only will be prevented from increasing in weight, but also from growing. This case is realized in experiment IV with dog A. In all probability, nearly all the reserve stuffs, all stored energy, in this animal were used up during the first period while the animal received only 110 calories, in the same manner as with dogs V or XI, where the fact was demonstrated by analysis.

We have seen by the foregoing considerations that, during the time of starvation, a considerable fraction of the energy required for maintenance is obtained from the energy stored in the body. However, this quantity is very limited. For instance, in the case of dog II it can not have amounted to more than 20 or 25 calories per day; in that of dog XI, to 10 calories at most. The amount of energy which the animals could draw from their own bodies is hardly sufficient to give them all the energy required according to the surface law. Furthermore, we see that dog A maintained its body weight of about 2,200 grams with an intake of only 170 calories, whereas 190 were required, and yet we must assume that this animal had no further reserve stuffs to burn. I have already mentioned that the values for energy required for maintenance obtained by the general formula seem to be at least 10 per cent higher than those found, for instance, by Rubner in some of his experiments. On the basis of these values dog A, weighing 2,200 grams, receives sufficient energy from 170 calories, but in the case of dogs II and XI, the intake of energy plus the highest possible amount obtained from the body itself can scarcely cover the requirement. I conclude that emaciated animals show a low demand for energy. The opposite opinion generally prevails, namely, that an emaciated young animal (child) needs more energy per kilo for maintenance than a well-nourished one. (Lissauer, Schlossmann.)

In the Philippine Islands the prevailing temperature may have an influence. Emaciated animals in a temperate climate, where they are kept at from 15° to 20°, possibly may lose more heat and therefore require more energy for maintenance than in Manila, where the temperature rarely falls below 25°. At the time dog VI was most emaciated, the temperature varied between 28° and 35°. This point is worth mentioning because it may explain certain divergencies.

BIOLOGICAL CONSIDERATIONS CONCERNING THE SUPPRESSION OF GROWTH BY RESTRICTING THE FOOD.

In the course of our experiments we could distinguish two periods: *First period.* As long as there is a reserve of energy in the body, the animal draws on this and, while starving parts of the body, continues to grow. This "starvation" does not produce a loss in weight as it would with an adult animal, but is compensated, or even overcompensated for by an increase in the weight of the skeleton and by an increase of the water content of the body. (Verwässerung.) *Second period.* This begins when the animal has reached the last stage of emaciation, in which, if the intake of energy only meets the demand required for maintenance, no growth takes place and both weight and growth are at a standstill.

During the first period, constancy or slight increase of weight indicates inanition, during the second period, cessation of growth.

It is only possible to suppress growth entirely by restricting the food when an animal is so emaciated that it has no further reserve stuffs to draw on. From a biological standpoint there are two forces in a growing animal which to a certain extent oppose each other, the tendency to grow and the tendency to maintain life. (Erhaltungstrieb.)

In the first periods of the experiments it appears that the tendency to grow in a young animal is greater than the tendency to maintain life. The further course of the experiments shows that the tendency to maintain life finally secures the upper hand. Therefore, the tendency to maintain life appears to be the greater biologic power. This observation is fully in accord with the results of investigations by Moreschi.[10] This author, at the suggestion of Ehrlich, studied the influence of a restriction of food on tumors in mice. He found that by a suitable restriction of food the growth of a tumor could be suppressed, that the tendency of the tumor to grow is not greater than the tendency to maintain life in the animal. Of course, this may depend on the malignancy of the tumor; in his experiments the power of the tumor-cells to attract material of nutrition was not greater than that of the normal tissue-cells.

We find similar conditions in our experiments: While the bones attract food material with great power, in order to grow, this tendency is finally overcome by that of the animal to maintain its life.

Some observations made by Waters and mentioned above, which lead to very similar conclusions, may be quoted here.

> This author says that "ungrown animals that had been previously well nourished continued to increase in height and in width of hip for a considerable length of time, even though on a starving ration. Apparently, the animal organism is capable of drawing upon its reserve for the purposes of sustaining the growth process for a considerable time and to a considerable extent. Our experiments indicate that after the reserve is drawn upon to a certain extent to support growth, the process ceases and there is no further increase in height or in length of bone. From this point on, the animal's chief business seems to be to sustain life. This law applies to animals on a stationary live weight as well as to those being fed so that the live weight is steadily declining, and, indeed, to those whose ration, while above maintenance, and causing a gain in live weight, is less than the normal growth rate of the individual. Such an animal will, while gaining in weight, get thinner, because it is drawing upon its reserve to supplement the ration in its effort to grow at a normal rate."

We see from our experiments that the skeleton of all parts of the body has the strongest "tendency to grow." While the other portions not only do not increase, but lose constantly during the time when the animal maintains itself by burning its fat and muscle tissue, the bones increase in weight and size. Indeed, we find the paradox that while protein in the muscles diminishes in quantity, that of the bones increases. The brain, from what we have seen, also seems to have an intensive tendency to grow. The other internal organs also have doubtless a sufficient tendency, at least to maintain themselves. The muscles suffer a greater reduction than any other part of the body, and seem to have no real tendency to grow. They follow the skeleton whenever the nutrition is favorable enough to permit such growth, and the conclusion could be drawn that their growth is controlled rather by mechanical forces (traction) than by an internal force (tendency to grow).

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[10] *Ztschr. f. Immunitätsforsch. u. exp. Ther.* (1909), 2, 651.

ENERGY REQUIRED DURING GROWTH.

A short discussion of the behavior of the dogs which were amply fed is also necessary. For the purpose of calculating what fraction of the energy taken with the food was used for growth, we will take the average weight of the dog as a basis for the calculation of the energy required for maintenance. The excess of calories over this amount can be regarded as being used for the production of new body substances in a more or less economic way. As "optimal growth" we may term with Rubner the condition under which the greatest percentage of this excess of calories is transformed into new body substances. No one of our dogs probably was at this stage of optimal growth, but all of the animals were more or less overfed, and hence the number of calories used for the formation of 1 gram of new body substances was higher than at the stage of optimal growth.

I have calculated, in the way just described, the number of calories used for the production of 1 gram of new body substance for certain periods of our experiments. It seems advisable as a basis for such calculations to take periods as long as possible, in order to reduce the unavoidable error due to the daily variations of the live weight. The values obtained vary from about 1.6 to 4.6 calories (see the following table). The higher values, 3 to 4 calories, are found when the animal is amply fed and toward the end of an experiment when the animal is older. This will easily be understood if we assume that under these circumstances there is a relatively greater deposition of fat tissue, representing a higher caloric value.

Number of calories used for the production of 1 gram of new body substance in dogs.

Dog No.	In days.	From—	To—	Daily increase in weight.	Energy in food.	Energy for maintenance.	Difference.	Energy consumed for 1 gram growth.
		Grams.	*Grams.*	*Grams.*	*Calories*	*Calories*	*Calories*	*Calories.*
I	20	2,660	3,380	69	425	250	175	2.6
IV	10	2,290	2,670	28	340	210	130	4.6
IV	10	2,670	2,950	28	340	230	110	4.0
C	35	2,700	3,340	18	300	245	55	3.0
B	30	1,715	2,250	15.5	225	170	55	3.5
VIII	50	1,265	2,045	15.6	190	165	25	1.6
XII	50	1,572	2,532	19.0	215	185	30	1.6

Several authors (Oppenheimer,[20] Rubner, Graham-Lusk[21] and Wilson[22]) have attempted to formulate mathematical laws concerning the relation of the caloric intake to the increase in body weight. Rubner states that all young mammals, with the exception of man, in their first days of life need the same number of calories (4,808) to increase their body weight 1 kilo. This law would apply to a time when the food supply of the animal is controlled by nature, and we could understand a universal law under such conditions. However, it has already been shown that a number of Rubner's data are quite arbitrarily selected and that others, equally reliable, lead to different results.

Oppenheimer has observed that the growth in grams of normal, breast-fed children of the same age may be nearly proportional to the quantity of milk ingested.

This question has also been studied by Graham-Lusk, who, from his own experiments on suckling pigs performed in connection with Wilson, and from older experiments on dogs done by Rost,[23] has shown that, "during the normal development of the young of the same age and species, a definite percentage of the food (expressed in the caloric value) is retained for growth irrespective of the size of the individual."

While it is difficult to give a satisfactory explanation for this law from the standpoint of energetics, it seems to hold true in practice. For instance, Bamberg,[24] in a recent investigation on young pigs fed with the same milk, has obtained results from which we might also find a confirmation of Graham-Lusk's law:

Number of pig.	First five weeks of experiment.			
	Weight at start.	Increase	Quantity of milk.	$\frac{J}{Q}$
	Grams.	*Grams.*	*Grams.*	
C	1,963	5,004	4,621	1.08
D	1,743	3,557	3,469	1.02
E	1,850	2,632	2,344	1.12

In spite of the entirely different quantities of milk taken, there is a very surprising agreement between the quotients $\frac{J}{Q}$ which indicate the increase in weight per unit of food (milk).

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[20] *Ztschr. f. Biol.* (1909), **42**, 147.

[21] Science of Nutrition, Philadelphia & London, 2. ed. (1909), 247ff.

[22] *Am. Journ. Physiol.* (1902), **8**, 197, 212.

[23] *Arb. a. d. kais. Gsndhtsmte.* (1901), **18**, 206.

[24] *Jahrb. f. Kinderheilk.* (1910), **71**, 670.

I obtain figures confirming this rule from some of my experiments on amply fed dogs. If we compare the figures for a period of fifty days the following values are obtained:

Dog.	Calories.	Increase.		Increase.	Calories taken per gram increase.
		From—	To—		
		Grams.	*Grams.*	*Grams.*	
B	19,950	2250	3820	1,570	12.7
C	13,925	2220	3220	1,000	13.9
VIII	9,500	1265	2045	780	16.4
XII	10,750	1785	2623	838	15.6

However, if we compare the well and poorly nourished dogs of the same litter, the law does not hold. It seems clear that an animal gaining 1,000 grams during fifty days needs fewer calories for this gain than one gaining 1,000 grams in one hundred or one hundred and fifty days. In the first instance the animal needs to be maintained for only one-half the time as in the latter. Therefore, it seems nearly impossible to give any mathematical law, so long as the time factor can be varied freely.

INCREASE IN WEIGHT AS AN INDEX TO GROWTH WITH SPECIAL REFERENCE TO CHILDREN.

One of the most striking results of our experiments is the demonstration that lack of increase in weight in a growing animal does not indicate a lack of growth, but starvation, accompanied by loss of body substances.

This is of importance in practical pediatrics. We learn from it that a child which does not increase in weight or increases slowly is so undernourished that part of its own body substances are being consumed. We can go even further in our conclusions. If a child does not present the weight which we have a right to expect at its age, assuming that it was born with a more or less normal weight, this child's body does not have the normal composition. It will contain a higher percentage of bones, a lower content of fat and muscle tissues, and a higher content of water and the caloric value of a unit of its body weight will be below that of a normal child. To feed such a child properly it is necessary first to attempt to replace water in its body by fat and protein. Therefore, it can use energy above the amount required for maintenance without increasing in weight, or, for a certain increase in weight it will need more food than a normal child of the same weight. This explanation, based on our observation of "Verwässerung" as a consequence of continuous undernourishment, may give us the key to the understanding of a very remarkable fact recently reported by students of pediatrics and already mentioned in this paper. As Rosenstern[25] and others have shown and as I can demonstrate from my own observations, a child of a weight considerably lower than that which corresponds to its age will need a higher intake in calories per kilo for a normal increase in weight than either an infant of the same weight but younger, or one of the same age but heavier (normal weight).[26] This conclusion can best be shown by the following charts, which figure the food given and the weight observed in children of nearly the same weight but of different ages.

These observations are taken from milk-feeding stations established by the Bureau of Public Instruction in connection with public schools and conducted by Miss J. Jackson, under the supervision of the writer. I am indebted for the use of the following data to Miss Jackson who made up the milk daily for the children and observed them during the week, while only weekly inspections were made by the writer when the weights were taken.

Two characteristic examples are cited.

MARIA INOCENCIO.

From week—	To week—	Number of days.	Increase			Calories	
			From—	To—	Per day.	Per day.	Per kilo.
			Grams.	*Grams.*	*Grams.*		
21	26	35	3,500	3,600	3	350-375	100-105
26	31	31	3,650	4,225	17	450-120	115-120
31	35	28	4,225	4,811	21	500	125

MIGUELA PRIEGA.

4	9	35	3,550	4,175	17	350-400	100
9	13	28	4,175	4,850	24	450-475	105

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[25] *Deutsche med. Wchnschr.* (1909), **35**, 295.

[26] Finkelstein and other authors advise that a child be given the number of calories that correspond to its age, irrespective of its weight.

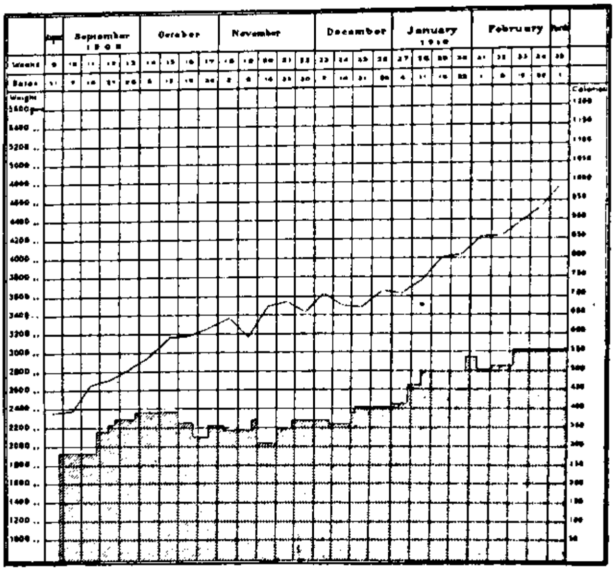


CHART 5.—Showing weight and food of Maria Inocencio.

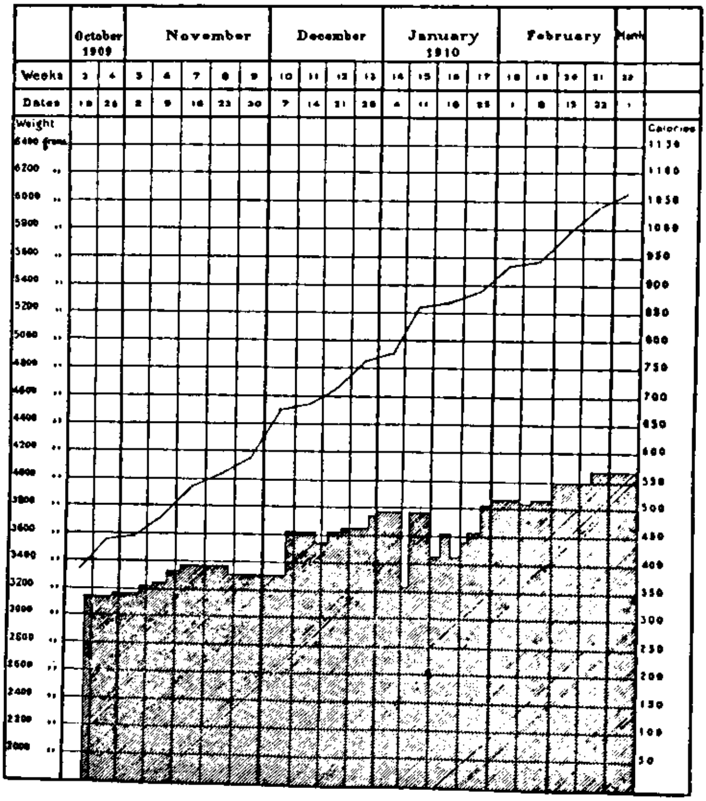


CHART 6.—Showing weight and food of Miguela Priega.

Maria Inocencio increased less than 5 grams per day, on a daily intake of from 100 to 105 calories per kilo, but 17 grams per day on a daily intake of from 115 to 120 calories per kilo, and she needed 125 calories per day to increase 27 grams per day. This child at the time of observation was from twenty to thirty weeks of age. The other child of the same weight, but only nine to fourteen weeks of age, with an intake of 95 calories per kilo increased about 17 grams per day, and with one of about 105 calories per kilo it increased 24 grams per day.

The question as to how far a continuous restriction in food, a constant undernourishment, may influence not only a single individual but entire nations and races, is doubtless very interesting and of unusual importance in the Philippine Islands. My experiments are not far enough advanced to justify conclusions concerning the possible influence of underfeeding upon offspring. The investigation of this question on mammals will necessarily require a long time. However, my work so far seems to indicate that a constant undernourishment will inhibit to some extent the normal development of the individual.

CONCLUSIONS.

The most important results of my experiments may be summarized as follows: A growing animal which receives only sufficient food to keep its body weight constant, or to allow a slight increase, is in a condition of severe starvation. If by a restriction of food the increase in weight is inhibited, the skeleton grows at the expense of other parts of the body, especially of the flesh. Most of the organs retain their weight and size, while the brain grows to reach its normal weight. The composition of the body—when at a constant weight—undergoes remarkable changes: Fat is consumed more or less entirely, the quantity of protein, especially of the muscles but not of the organs, is diminished and a great proportion of the body tissues is replaced by water; thus, this water and the increase of the skeleton together, replace the body materials lost. The caloric value of 1 gram body weight of an animal which has undergone such a process to its extreme limit may amount to only one-third of the normal value.

It is possible by supplying suitable amounts of food to maintain a dog in an emaciated condition, apparently in good health, and at the weight of a puppy, for nearly one year, while its weight at the end of the year should be three times as great. If such an animal is thereupon fed amply, it fattens and rounds out, but does not reach the size of a control animal which from the beginning has been normally fed. It is unable to make good the growth suspended by the long restriction of food.

The "growth" principally depends on the tendency to grow possessed by the skeleton. The skeleton loses its capability of growing in more advanced age regardless of the size which the animal has reached.

I wish to thank Mr. Pio Valencia, formerly demonstrator in physiology, for his kindness in watching the animals when I was absent from Manila.

RECORDS OF EXPERIMENTS NOS. I–IV, SHOWING LIVE WEIGHT AND FOOD OF DOGS.

TABLE 14, EXPERIMENT I.—*Live weight and food of dogs I, II, III, and IV.*

Date.	Day of experiment.	Dog I.		Dog IV.		Dog II.		Dog III.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1909.									
January 20	1	1,435	124	1,430	124	1,419	80	1,390	80
January 25	6	1,465	236	1,570	236	1,410	125	1,310	110
January 30	11	1,710	285	1,730	285	1,480	130	1,330	110
February 4	16	1,995	(270)	2,090	(260)	1,575	95	1,510	(?)
February 9	21	Sick	290	2,100	305	Sick.	(?)	Sick.	110
February 14	26	2,235	340	2,290	330	1,705	85	1,735	110
March 19.	31	2,475	370	2,560	350	1,840	85	1,715	90
February 24	36	2,660	340	2,670	330	1,810	80	1,720	85
March 1	41	2,800	380	2,760	350	1,865	80	1,750	80
March 6	46	3,100	380	2,950	355	1,910	80	1,780	80
March 11	51	3,220	380	3,060	355	1,830	80	1,780	80
March 16	56	3,380	380	2,990	355	1,950	80	1,800	80
March 21	61	3,560	425	----	----	----	----	----	----
March 26	66	3,850	425	----	----	----	----	----	----
April 1	71	4,250	425	----	----	----	----	----	----
April 6	76	4,410	425	----	----	----	----	----	----
April 11	81	4,420	425	----	----	----	----	----	----

TABLE 15, EXPERIMENT II.—*Live weight and food of dogs V and VI.*

Date.	Dog V.						Dog VI.				
	Day of experiment.	Weight.	Number of days.	Meat.	Starch.	Calories.	Weight.	Number of days.	Meat.	Starch.	Calories.
1909.				*Gms.*	*Gms.*		*Grams.*		*Gms.*	*Gms.*	
February 19	1	3,340	50	210	21	420	3,260	50	70	7	140
February 24	6	3,345					3,210				
March 1	11	3,805					3,320				
March 5	16	Sick.					3,340				
March 11	21	3,820					3,380				
March 16	26	4,000					3,410				
March 21	31	4,040					3,310				
March 26	36	4,280					3,310				
March 31	41	4,400					3,315				
May 5	46	4,620					3,495				
April 10	51	4,610	50	170	17	335	3,430	50	75	75	150
April 15	56	4,720					3,520				
April 20	61	4,850					3,545				
April 20	66	4,850					3,560				
April 30	71	5,020					3,540				
May 5	76	5,090					3,560				
May 10	81	5,310					3,555				
May 15	86	5,340					3,510				
May 20	91	5,300					3,500				
May 25	96	5,370					3,500				
May 30	101	5,380					3,530				
June 4	106	5,320	7	112	45	335	3,500	7	45	18	135
June 9	111	5,370	13	120	48	360	3,590	92	40	16	120
June 14	116	5,275					3,400				
June 19	121	5,285					3,430				
June 24	126	5,260	10	140	56	420	3,210				
June 29	131	5,220					3,310				
July 4	136	5,290	77	160	64	480	3,375				
July 9	141	5,280					3,330				
July 14	146	5,320					3,240				
July 19	151	5,310					3,150				
July 24	156	5,445					3,030				
July 29	161	5,610					3,000				
July 3	166	5,690					2,870				
July 8	171	5,815					2,880				
July 13	176	5,950					2,835				
July 18	181	5,805					2,835				
July 23	186	5,860					2,830				
July 28	191	5,780					2,950				
May 2	196	5,775					2,830				
September 7	201	5,750					2,850				
September 12	206	5,880					[b]2,850	3	50	20	150
September 14	208	[a]5,885									

[a] Two hundred and eighth day.

[b] Two hundred and third day.

TABLE 16, EXPERIMENT III.—*Live weight and food of dogs VIII, XI, XII, and XIV.*

Day of experiment.	Date.	Dog VIII.		Dog XI.		Dog XII.		Dog XIV.	
		Weight.	Food.	Weight.	Food.	Weight.	Food.	Weight.	Food.
	1909.	*Grams.*		*Grams.*		*Grams.*		*Grams.*	
1	February 25	585	10 days 130 calories	760	20 days 110 calories	860	21 days 225 calories	732	21 days 110 calories
6	March 2	675		800		942		773	
11	March 7	720	8 days 165 calories	875		1,150		780	
16	March 12	840	4 days 200 calories	905		1,277		805	
21	March 17	990	23 days 180 calories	950		1,400	22 days 205 calories	866	22 days 70 calories
26	March 22	1,055		975	25 days 90 calories	1,482		917	
31	March 27	1,125		980		1,572		915	
36	April 1	1,177		973		1,650		935	
41	April 6	1,265		1,040		1,785	52 days 215 calories	945	
46	April 11	1,342	50 days 190 calories	1,089	50 days 95 calories	1,845		923	48 days 75 calories
51	April 16	1,415		1,037		1,840		930	
56	April 21	1,500		1,044		1,912		944	
61	April 26	1,570		1,122		2,052		1,000	
66	May 1	1,671		1,185		2,179		1,020	
71	May 6	1,742		1,235		2,347		1,040	
76	May 11	1,820		1,270		2,460		1,070	
81	May 16	1,932		1,300		2,532		1,040	
86	May 21	1,982		1,340		2,605		1,015	
91	May 26	2,045	6 days 195 calories	1,306	15 days 90 calories	2,623	5 days 225 calories	[4]915	
96	May 31	2,050		1,355		2,760	10 days 230 calories	-------	
101	June 5	2,100	12 days 180 calories	1,240		2,790		-------	-------

106	June 10	2,105	32 days 240 calories	1,230	25 days 100 calories	2,780	30 days 250 calories		
111	June 15	2,225		1,825		2,790			
116	June 20	2,120		1,195		2,835			
121	June 25	2,120		1,160		2,865		----	----
126	June 30	2,290		1,160		2,925			
131	July 5	2,297		[b]1,070		3,028			
136	July 10	2,290		----		[c]2,990			
141	July 15	[a]2,345	----	----	----	----	----	----	----
146	July 20	----	----	----	----	----	----	----	----

[a] Killed one hundred and forty-sixth day; 2,375 grams.

[b] Killed one hundred and thirty-sixth day; 1,100 grams.

[c] Killed one hundred and forty-first day; 3,000 grams.

[d] Ninety-first day died; 915 grams.

TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, B, C, and D.*

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1909.		*Grams.*		*Grams.*		*Grams.*		*Grams.*	
August 1	1	1,250	340	1,380	225	1,520	225	1,295	340
August 6	6	1,340	340	1,450	225	1,580	225	1,360	340
August 11	11	1,330	340	1,480	225	1,580	225	1,425	340
August 16	16	1,465	300	1,520	225	1,640	225	1,485	340
August 21	21	1,490	225	1,590	225	1,700	225	1,500	340
August 26	26	1,505	225	1,605	170	1,745	150	1,515	225
August 31	31	1,705	225	1,715	200	1,935	110	1,700	225
September 5	36	1,770	110	1,780	225	1,890	110	1,840	225
September 10	41	1,860	110	1,860	225	1,920	110	1,900	225
September 15	46	1,950	110	2,020	225	1,940	170	[a]1,990	170
September 20	51	1,990	110	2,080	225	2,010	170		
September 25	56	1,935	110	2,150	250	2,040	200		
September 30	61	1,935	110	2,250	340	2,130	225		
October 5	66	1,960	110	2,500	400	2,320	250		
October 10	71	1,935	110	2,650	410	2,370	270		
October 15	76	1,935	110	2,830	410	2,490	270		
October 20	81	1,920	110	3,090	420	2,680	270		
October 25	86	1,850	135	3,180	440	2,700	300		
October 30	91	1,860	135	3,325	440	2,795	300		
November 4	96	1,900	135	3,525	440	2,935	300		
November 9	101	1,850	170	3,610	440	2,970	300		
November 14	106	1,915	170	3,720	460	3,095	300		
November 19	111	1,940	170	3,885	500	3,130	300		
November 24	116	2,045	170	4,010	500	3,220	300		
November 29	121	2,020	170	4,110	500	[b]3,340	300		
December 4	126	2,030	170	4,335	500				
December 9	131	2,015	170	4,460	500				
December 14	136	1,940	170	4,490	500				
December 19	141	1,960	170	4,595	500				
December 24	146	1,995	170	4,820	500				
December 29	151	1,990	170	5,010	500				
1910.									
January 3	156	2,000	170	5,050	500				
January 8	161	2,010	170	5,020	500				
January 13	166	2,015	170	5,120	500				
January 18	171	1,950	170	5,100	500				
January 23	176	2,010	170	5,260	500				
January 28	181	2,050	170	5,270	550				
February 2	186	2,110	170	5,450	570				
February 7	191	2,040	170	5,510	570				
February 12	196	2,090	170	5,520	570				
February 17	201	2,180	170	5,605	570				
February 22	206	2,080	170	5,825	570				
February 27	211	2,230	170	6,090	570				
March 4	216	2,050	170	6,145	570				

[a] Killed forty-ninth day.

[b] Died one hundred and twenty-third day.

TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, etc.*—Continued.

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1910.		*Grams.*		*Grams.*		*Grams.*		*Grams.*	
March 9	221	2,100	170	6,140	570	------	------	------	------
March 14	226	2,305	170	6,185	570	------	------	------	------
March 19	231	2,315	170	6,335	570	------	------	------	------
March 24	236	2,315	170	6,315	570	------	------	------	------
March 29	241	2,310	170	6,370	570	------	------	------	------
April 4	246	2,270	170	6,300	570	------	------	------	------
April 9	251	2,220	170	6,400	570	------	------	------	------
April 14	256	2,190	170	6,330	570	------	------	------	------
April 19	261	2,165	170	6,290	570	------	------	------	------
April 24	266	2,195	170	6,335	570	------	------	------	------
April 29	271	2,150	170	6,250	570	------	------	------	------
May 4	276	2,300	170	6,270	570	------	------	------	------
May 9	281	2,300	170	6,350	570	------	------	------	------
May 14	286	2,290	170	6,380	680	------	------	------	------
May 19	291	2,220	170	6,360	680	------	------	------	------
May 24	296	2,390	170	6,450	680	------	------	------	------
May 29	301	2,350	170	6,420	680	------	------	------	------
June 3	306	2,400	170	6,400	680	------	------	------	------
June 8	311	2,440	170	6,460	680	------	------	------	------
June 13	316	2,360	170	6,500	680	------	------	------	------
June 18	321	2,320	170	6,500	680	------	------	------	------
June 23	326	2,340	170	6,500	680	------	------	------	------
June 28	331	2,350	170	6,690	680	------	------	------	------
July 3	336	2,390	170	6,760	680	------	------	------	------
July 8	341	2,400	170	6,800	680	------	------	------	------
July 13	346	2,520	170	6,870	680	------	------	------	------
July 18	357	2,450	170	6,800	680	------	------	------	------
July 23	356	2,450	230	6,850	680	------	------	------	------
July 28	361	2,510	280	6,850	680	------	------	------	------
August 2	366	2,540	340	6,800	680	------	------	------	------
August 7	371	2,650	340	6,700	680	------	------	------	------
August 12	376	2,700	340	6,680	680	------	------	------	------
August 17	381	2,790	340	6,700	680	------	------	------	------
August 22	386	2,910	340	6,690	680	------	------	------	------
August 27	391	3,000	340	6,550	680	------	------	------	------
September 1	396	3,040	340	6,580	680	------	------	------	------
September 6	401	3,220	340	6,700	680	------	------	------	------
September 11	406	3,250	340	6,910	680	------	------	------	------
September 16	411	3,225	340	6,835	680	------	------	------	------
September 21	416	3,325	450	6,865	680	------	------	------	------
September 26	421	3,470	450	7,000	680	------	------	------	------
October 1	426	3,630	450	7,020	680	------	------	------	------
October 6	431	3,715	450	7,005	680	------	------	------	------
October 11	436	3,740	450	6,950	680	------	------	------	------
October 16	441	4,245	680	[*]7,060	680	------	------	------	------
October 21	446	4,390	680	7,060	680	------	------	------	------

[*] Both dogs receive equal amounts.

TABLE 17, EXPERIMENT IV.—*Live weight and food of dogs A, etc.*—Continued.

Date.	Day of experiment.	Dog A.		Dog B.		Dog C.		Dog D.	
		Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.	Weight.	Calories per day.
1910.		*Grams.*		*Grams.*		*Grams.*		*Grams.*	
October 26	451	4,550	680	7,010	680				
October 31	456	4,690	680	7,080	680				
November 5	461	4,810	680	7,045	680				
November 10	466	4,925	680	7,125	680				
November 15	471	4,995	680	7,250	680				
November 20	476	5,130	680	7,340	680				
November 25	481	5,290	680	7,430	680				
November 30	486	5,300	680	7,400	680				
December 5	491	5,435	680	7,365	680				
December 10	496	5,395	680	7,320	680				
December 15	501	5,440	680	7,400	680				

ILLUSTRATIONS.

PLATE I.

FIG. 1. Dog V of experiment II at the 175th day.
2. Dog VI of experiment II at the 175th day.

PLATE II.

FIGS. 1 and 3. Dog A of experiment IV.
2 and 4. Dog B of experiment IV.

PLATE III.

FIGS. 1 and 3. Dog A of experiment IV.
2 and 4. Dog B of experiment IV.

PLATE IV.

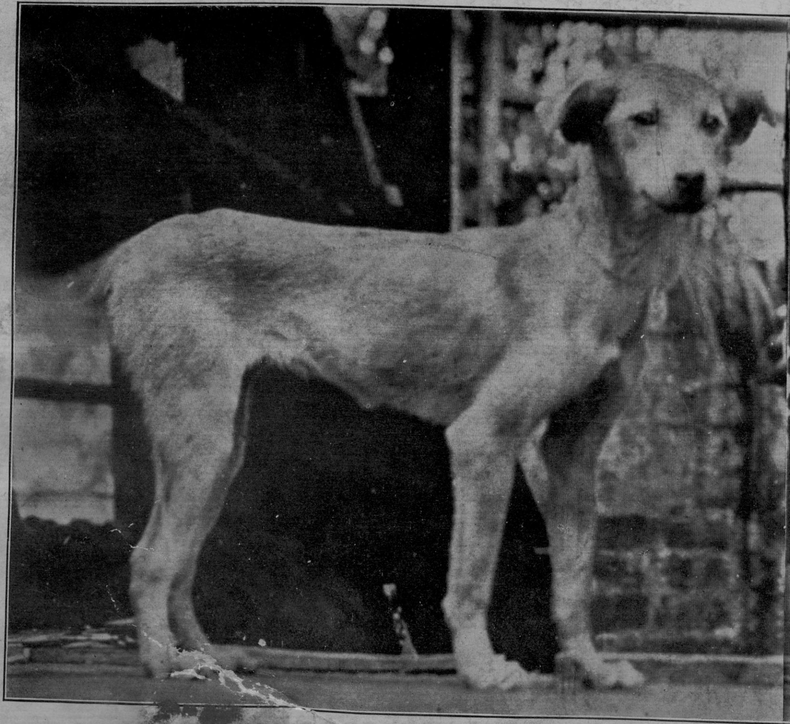
FIG. 1. Dogs used in experiment IV.
2. Some of the bones of dogs A and B used in experiment IV.

DIAGRAMS.

1. Composition of dogs II to VI of experiments I and II.
2. Percentage of water and solids in blood, brain, bones, and muscles of dogs V and VI of experiment II.
3. Composition of bones in dogs V and VI of experiment II.

CHARTS.

1. Variation in weights of dogs I to IV of experiment I.
2. Variation in weights of dogs V and VI of experiment II.
3. Variation in weights of dogs VIII, XI, XII, and XIV of experiment III.
4. Variation in weights and calories of dogs A to D of experiment IV.
5. Showing weight and food of Maria Inocencio.
6. Showing weight and food of Miguela Priega.



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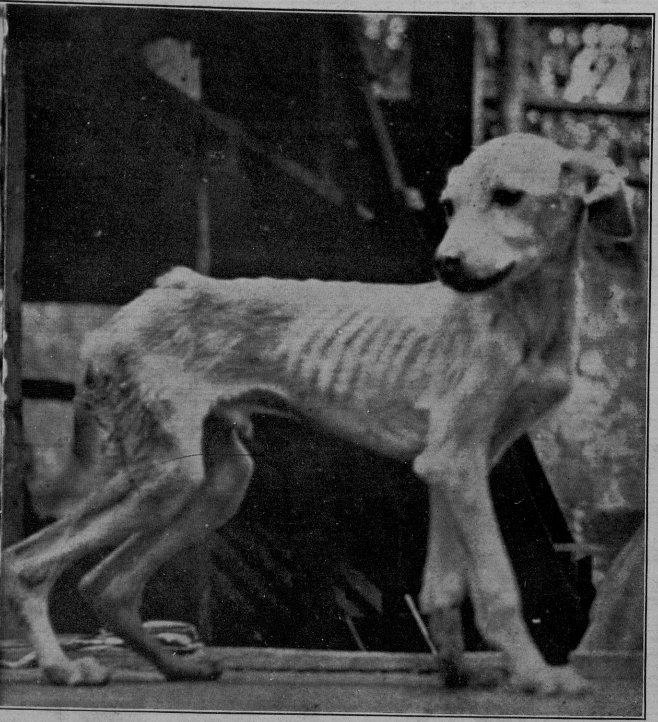


FIG. 2.

PLATE I.

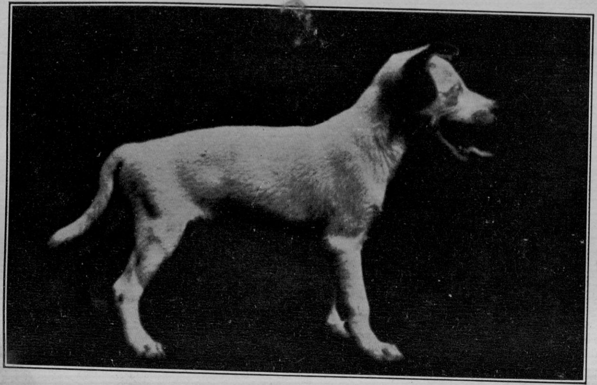


FIG. 1.

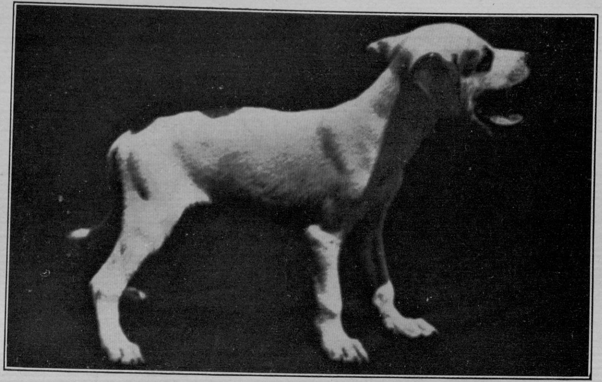


FIG. 2.

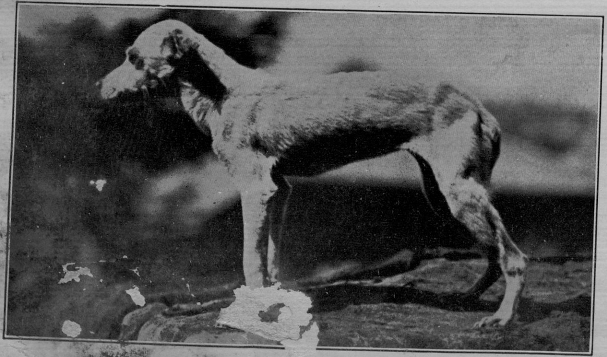


FIG. 3.

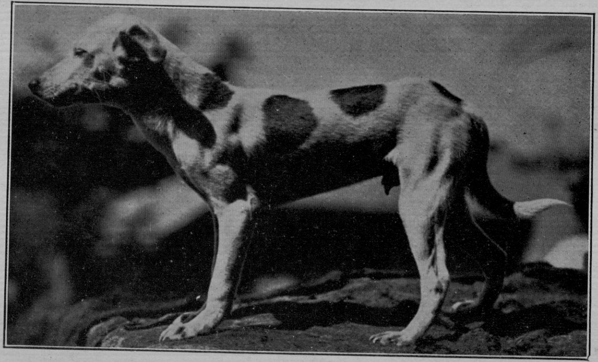


FIG. 4.

PLATE II.

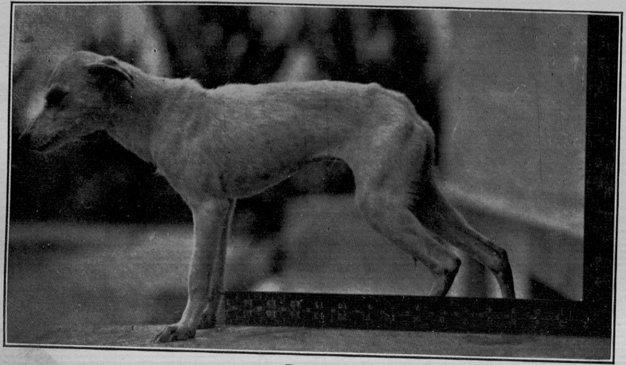


FIG. 1.

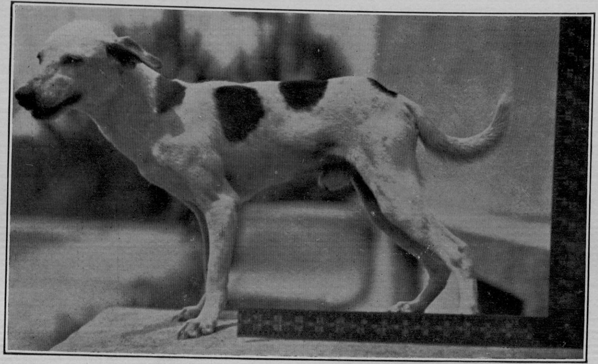


FIG. 2.

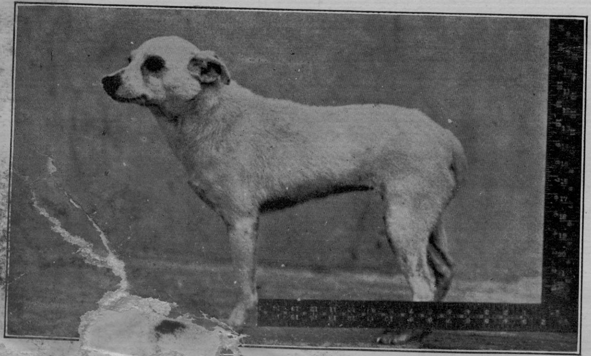


FIG 3.

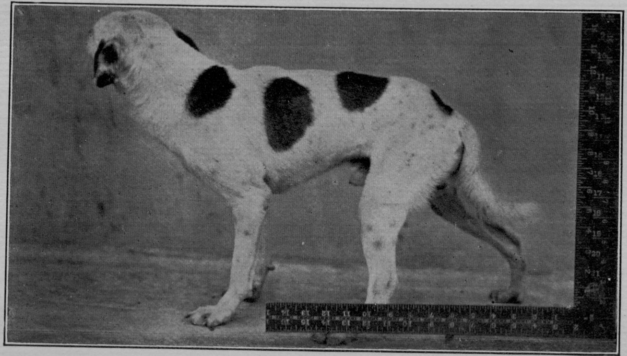
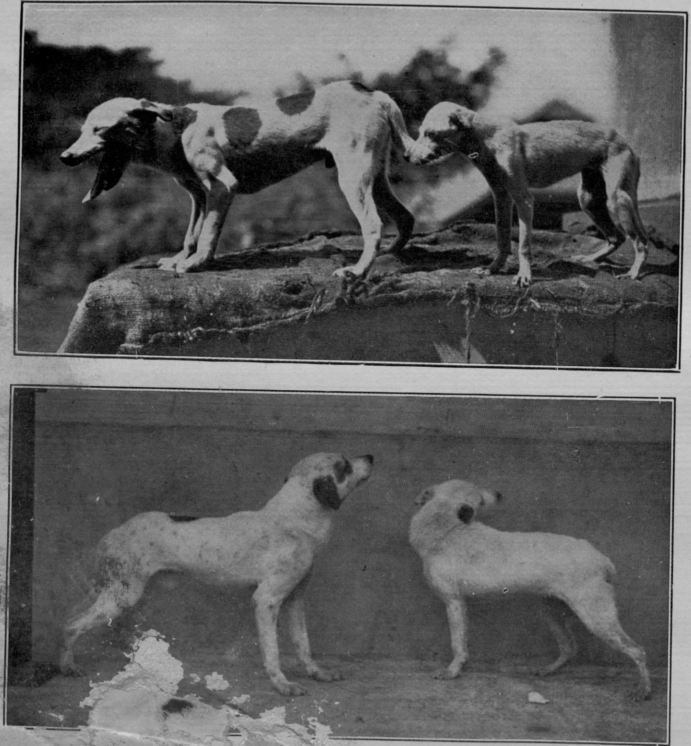


FIG. 4.

PLATE III.



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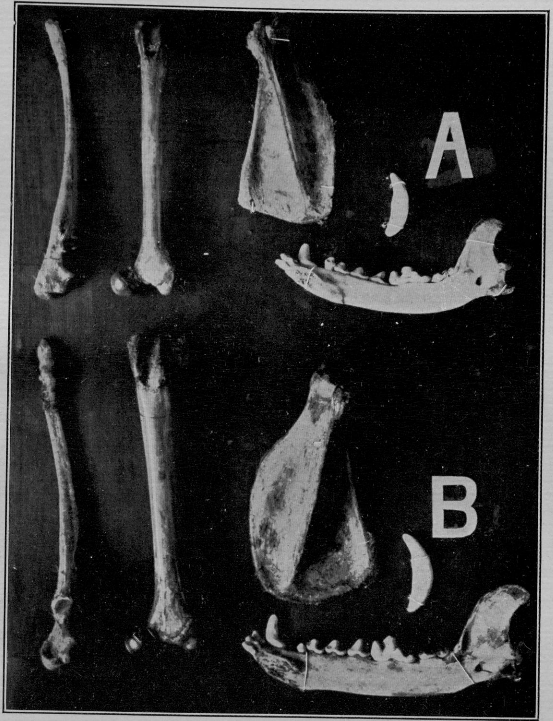


FIG. 2.

PLATE IV.

INDICATIONS OF ACID INTOXICATION IN ASIATIC CHOLERA.

By Andrew Watson Sellards and A. O. Shaklee.

(From the Biological Laboratory, Bureau of Science, and the Pharmacological Laboratory, College of Medicine and Surgery, University of the Philippines, Manila, P. I.)

The position of the theory of acid intoxication in clinical medicine rests almost entirely upon the investigations in one disease, namely, diabetes. More or less prominent symptoms of acid intoxication may develop in some other conditions, such as starvation, the toxæmia of pregnancy, and after general anæsthesia, but the knowledge derived from these sources is of relatively minor importance when compared with that obtained from diabetes. However, there are certain features in Asiatic cholera which afford an interesting opportunity for the study of acid intoxication.

An increase in the daily excretion of sulphuric acid and of ammonia in the urine together with the presence of β-oxybutyric acid has been reported by Hoppe-Seyler.(1) In a concluding note of this same article, Quincke reports a case of cholera in which 30 grams of sodium citrate were given by mouth and by rectum in the course of three days, but during this period the urine remained acid. V. Terray, Vas and Gara(2) found a considerable increase in the excretion of sulphuric and of phosphoric acids and also of ammonia and acetone. Acetoacetic acid was often present.

Perhaps the most important feature in cholera which bears upon acid intoxication is the increased tolerance of patients for alkalies. The intravenous injection of sodium bicarbonate in relatively large quantities often fails to render the urine alkaline. In the interpretation of this tolerance, the anuria of cholera, following the excessive loss of fluid by rectum, offers a possible complication. The alkalies introduced into the body might be excreted by other channels, for example by rectum. However, if quantities of 30 to 60 grams were being excreted into the intestine one would almost expect that the kidney also would excrete at least enough alkali to change the reaction of the urine. Moreover, if the alkali is retained in the body during the period of anuria, there is the possibility that it might be neutralized by substances other than acids, such as serum albumins for example. Therefore, in Table I the intervals between the injection of alkali and the first secretion of urine have been included. Five control cases are also added.

TABLE I.—*Intravenous injection of sodium bicarbonate in patients suffering from cholera.*

Serial number.	First injection.					Second injection.					
	Alkali.		Urine.			Alkali.			Urine.		
	Per cent.	Amount.	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	Interval between injections.	Per cent.	Amount.	Interval after alkali.	Cubic centimeters.	Reaction to litmus.
		Grams.	*Hours.*			*Hours.*		*Grams.*	*Hours.*		
1	0.5	10	No urine.		--------	7	0.5	10	16	50	Acid.
2	0.5	10	19	100	Acid.	26	1.5	15	15	160	Acid.
3	0.5	10	20	100	Acid.	29	1.5	15	12	230	Acid.
5	0.5	10	6	5	Acid.	24	0.5	10	1	100	Acid.
6	0.5	10	No urine.		--------	17	0.5	10	7	420	Acid.
7	0.5	10	No urine.		--------	11	0.5	10	4	60	Acid.
9	0.5	10	No urine.		--------	5	0.5	10	No urine.		--------
10	0.5	10	No urine.		--------	7	0.5	10	No urine.		--------
12	0.5	10	2¼	20	Acid.	5	0.5	10	1	80	Acid.
13	0.5	10	6	160	Acid.	--------	--------	--------	--------	--------	--------
14	0.5	10	No urine.		--------	6	0.5	10	8	200	Acid.
16	0.5	20	No urine.		--------	14	0.5	10	10	450	Acid.
17	1.5	30	1	5	Acid.	--------	--------	--------	3¼	200	Acid.
19	0.5	10	10¼	600	Acid.	--------	--------	--------	--------	--------	--------
20	0.5	10	15	100	Acid.	15	0.5	10	2	550	Acid.
21	0.5	10	No urine.		--------	22	0.5	10	2	220	Acid.

Serial number.	Third injection.						Fourth injection.					
	Alkali.			Urine.			Alkali.			Urine.		
	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.
	Hours.		*Grams.*	*Hours.*			*Hours.*		*Grams.*	*Hours.*		
1	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
2	26	0.5	10	6	220	Acid.	11	1.5	15	2	100	Acid.
3	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
5	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
6	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
7	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
9	4	0.5	10	No urine.		--------	7	0.5	10	8	(?)	Acid.
10	11	0.5	10	7	15	Acid.	8	1.5	15	8	140	Acid.
12	96	0.5	10	1	110	Acid.	--------	--------	--------	--------	--------	--------
13	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
14	15	0.5	10	2	250	Acid.	--------	--------	--------	--------	--------	--------
16	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
17	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
19	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
20	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
21	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------

TABLE I.—*Intravenous injection of sodium bicarbonate, etc.*—Continued.

Serial number.	Fifth injection.						Sixth injection.						Total amount of alkali.
	Alkali.			Urine.			Alkali.			Urine.			
	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	Interval between injections.	Per cent.	Amount	Interval after alkali.	Cubic centimeters.	Reaction to litmus.	
	Hours.		*Grams.*	*Hours.*			*Hours.*		*Grams.*	*Hours.*			*Grams.*
1	------	------	------	------	------	------	------	------	------	------	------	------	20
2	------	------	------	------	------	------	------	------	------	------	------	------	50
3	------	------	------	------	------	------	------	------	------	------	------	------	25
5	------	------	------	------	------	------	------	------	------	------	------	------	20
6	------	------	------	------	------	------	------	------	------	------	------	------	20
7	------	------	------	------	------	------	------	------	------	------	------	------	20
9	22	1.5	15	1	130	Alkaline.	------	------	------	------	------	------	55
10	9	1.5	15	12	70	Acid.	12	1.5	30	12	120	Acid.	90
12	------	------	------	------	------	------	------	------	------	------	------	------	30
13	------	------	------	------	------	------	------	------	------	------	------	------	10
14	------	------	------	------	------	------	------	------	------	------	------	------	30
16	------	------	------	------	------	------	------	------	------	------	------	------	30
17	------	------	------	------	------	------	------	------	------	------	------	------	30
19	------	------	------	------	------	------	------	------	------	------	------	------	30
20	------	------	------	------	------	------	------	------	------	------	------	------	10
21	------	------	------	------	------	------	------	------	------	------	------	------	20
													20

Control cases for Table I.

No.	Alkali.			Urine.					
	Per cent.	Cubic centimeters of solution.	Amount.	Interval after alkali.	Reaction to litmus.	Interval after alkali.	Reaction to litmus.	Interval after alkali.	Reaction to litmus.
			Grams.	*Hours.*		*Hours.*		*Hours.*	
1	1.5	300	4.5	1	Alkaline.	2	Acid.	--------	
2	1.5	200	3.0	2	Acid.	5	Acid.	12	Acid.
3	0.5	400	2.0	1	Alkaline.	3	Acid.	--------	
4	0.5	500	2.5	2¼	Acid.	3	Alkaline.	5	Acid.
5	0.5	1,000	5.0	1	Alkaline.	3	Alkaline.	10	Acid.

Recovery took place in all of the cases which are recorded in Table I. There were also four fatal cases; two died during the first day in the hospital without excreting any urine and in the remaining two, the first samples of urine following the injection of alkali were lost. Of the sixteen cases which are recorded, there was but one in which the urine had an alkaline reaction; the quantities of sodium bicarbonate which were administered varied from two to eighteen times the maximum amount which was required to render the urine alkaline in the control cases.

As regards the increased excretion of ammonia in the urine, we have observed that occassionally the injection of rather large amounts of alkali does not reduce the ammonia out-put. A similar result may also occur in diabetes.(3)

Suppression of urea.—The first specimens of urine voided after a period of anuria are often found to contain subnormal amounts of urea. If the test is made with sodium hypobromite, it also shows that the content of ammonium salts as well may be relatively low in the first specimens. The explanations which suggest themselves may be considered under the two general heads, i. e. there may either be retention of urea by the organism or there may be a diminished production. In cases where there is suppression of urine, an acute nephritis is always present and one must consider the possibility of retention of urea on account of the kidney lesion. On the other hand, the nitrogen which is ordinarily transferred to the production of urea, might be diverted for the neutralization of acids. Lastly, a diminished production of urea might result from an impairment in the function of the urea-forming organs. A few data have been collected which have some bearing on these possible explanations.

Excretion of urea by the kidneys.—The possibility of retention of urea in the body was first considered. No determinations were made with the purpose of detecting an accumulation of urea in the blood or other tissues. Instead of this, urea was injected intravenously into patients who showed a well-marked suppression of urea, the object being to determine whether the lesions of the kidney were sufficient to prevent the excretion of urea, provided it were present in the blood. Previous determinations had shown that, in patients treated with sodium chloride, the urea, after a period of partial suppression, returns very gradually to normal. Only a limited number of cases were tested. In order to avoid a sudden spontaneous increase in the urea excretion, very severe cases were selected in which recovery, if it occurred at all, would be relatively slow. The urea in solid form was added directly to two liters of Ringer's solution and in every instance the injection was made intravenously. Relatively small amounts of urea were employed, the maximum being 10 grams. All of the cases showed a very acute nephritis in addition to the suppression of urea. The severity of the cases selected made it improbable that any spontaneous increase in the excretion of urea would take place. Four cases were obtained which were suitable for injection. The protocols are as follows:

The first patient (number 4) was admitted in partial collapse. During the first thirty hours in the hospital he received three intravenous injections of 2 liters each of Ringer's solution of which the third contained 10 grams of urea. The records of the excretion of urea are given in Table II.

TABLE II.—*Injection of urea, case No. 4.*

Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
Hours.			
----------	[a]30	0.1	0.03
Injection of 10 grams of urea.[b]			
9	30	0.5	0.15
5¼	50	0.6	0.30
9½	80	1.7	1.36
5	120	0.9	1.08
9	90	1.2	1.08
8	250	1.8	4.50
5	120	1.4	1.68
14½	10	0.1	0.01
Death after seventeen hours.			

[a] Preceded by anuria for twenty-seven hours.

[b] This injection was made four and one-half hours after the first specimen of urine was obtained. Catheterization showed no urine at the time of injection.

The volume of urine and the percentage and amount of urea are given, since the interpretation of the data is a little complicated because of the variation in the time intervals and the quantities of urine excreted. On the third day after admission, a fourth injection of two liters of Ringer's solution was given. Death occurred on the fifth day of the disease with symptoms both of toxæmia and uræmia. In the two and one-half days after the injection of urea a total of 10.1 grams of urea was excreted. Assuming that the percentage of urea would not have increased spontaneously, we may calculate the natural percentage for this period as 0.1, i. e. the per cent found before any urea was injected; on this basis we may deduct 0.8 gram as the amount which naturally would have been excreted leaving 9.3 grams as the increase due to injection. In addition to this amount there were also two specimens of urine which were lost by involuntary micturition, i. e. only 8 of 10 specimens were obtained. We may estimate, then, that about 90 per cent of the injected urea was excreted within two and one-half days.

A second case (number 11) required 8 liters of Ringer's solution intravenously during the stage of collapse. Two grams of urea were added to the third and 8 grams to the fourth injection. The period of reaction set in at the beginning of the fourth day and a fifth injection of two liters of Ringer's solution was given for its possible effect on the urine. Death occurred on the fifth day with symptoms of toxæmia and uræmia. During the first day, after the first injection of 2 grams a total of only 0.68 grams of urea was obtained and after the 8 gram quantity, only 2.6 grams were recovered although of the 4 voidings following the second injection one was involuntary and the specimen was lost. Hence in this case not more than one-third of the urea which we injected was recovered. The data are given in Table III.

TABLE III.—*Injection of urea, case No. 11.*

Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
Hours.			
----------	[a]70	0.1	0.07
13½	110	0.1	0.11
3	40	0.1	0.04
Injection of 2 grams of urea.			
4	60	0.1	0.06
13½	230	0.15	0.35
9	180	0.15	0.27
Injection of 8 grams of urea.			
5½	160	0.3	0.48
8	120	0.1	0.12
16	340	0.6	2.04
Death after six hours.			

[a] Preceded by anuria for twenty-eight hours.

In a third case (number 18) 5 grams of urea were added to the third injection of Ringer's solution. The patient died in uræmia, one and one-half days later. During this period a total of 1.7 grams of urea were recovered. The number of samples lost by involuntary micturition was unavoidably large, only about half of the specimens being obtained. The data are to be found in Table IV.

TABLE IV.—*Injection of urea, case No. 18.*

Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
Hours.			
----------	[a]100	0.25	0.25
Injection of 5 grams of urea.[b]			
3	60	0.5	0.30
6	50	0.2	0.10
9½	100	0.7	0.70
2½	15	0.11	0.02
5	80	0.25	0.20
2	85	0.3	0.25
Death after nine hours.			

[a] Preceded by anuria for nineteen hours.

[b] This injection was made one and one-half hours after the first specimen of urine was obtained. Catheterization showed no urine at the time of injection.

In a fourth case, number 15, death occurred thirty-six hours after injection without any definite changes in the excretion of urea. Two specimens of urine were obtained during the stage of collapse, the urea falling from 0.6 per cent in the first to 0.05 per cent in the second. Then after a period of twenty-one hours of anuria, 8 grams of urea were injected. Two specimens of urine were obtained before death. The first one of 20 cubic centimeters contained 0.6 per cent of urea. This was obtained one and one-half hours after the injection. A second specimen measuring 10 cubic centimeters was obtained fifteen hours later. It contained 0.25 per cent of urea.

As regards control patients, fatal cases have been frequently observed in which the variation in the urea content was very slight. A typical record of such a case is given in Table V. A patient dying in uræmia has been selected since more or less pronounced symptoms of uræmia were present in the four cases injected with urea.

TABLE V.—*Control with sodium chloride.*

Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
Hours.			
----------	[a]75	0.2	0.15
13	100	.1	.10
13¼	90	.15	.13
18	80	.3	.24
14	65	.2	.13
10	70	.4	.28
Death after twelve hours.			

[a] Preceded by anuria for forty-four hours.

Of the four cases injected with urea, there is one (Table II) in which a definite result was obtained. After the injection of urea, the percentage of urea increased eighteen-fold; then after a quantity equivalent to about 90 per cent of the amount injected had been excreted, the urea content fell to the same percentage that was found before the injection. This case would indicate that the suppression of urea is not always due to nephritis. The observations on this patient were carried out principally during the stages of collapse and reaction before symptoms of uræmia were prominent. The other three cases (numbers 11, 15 and 18) indicate that the behavior of this patient does not represent the usual result following the injection of urea, partly perhaps because of the difficulty of obtaining suitable cases for carrying out a complete test, or perhaps the urea in these three cases was used in the neutralization of acids before excretion could take place.

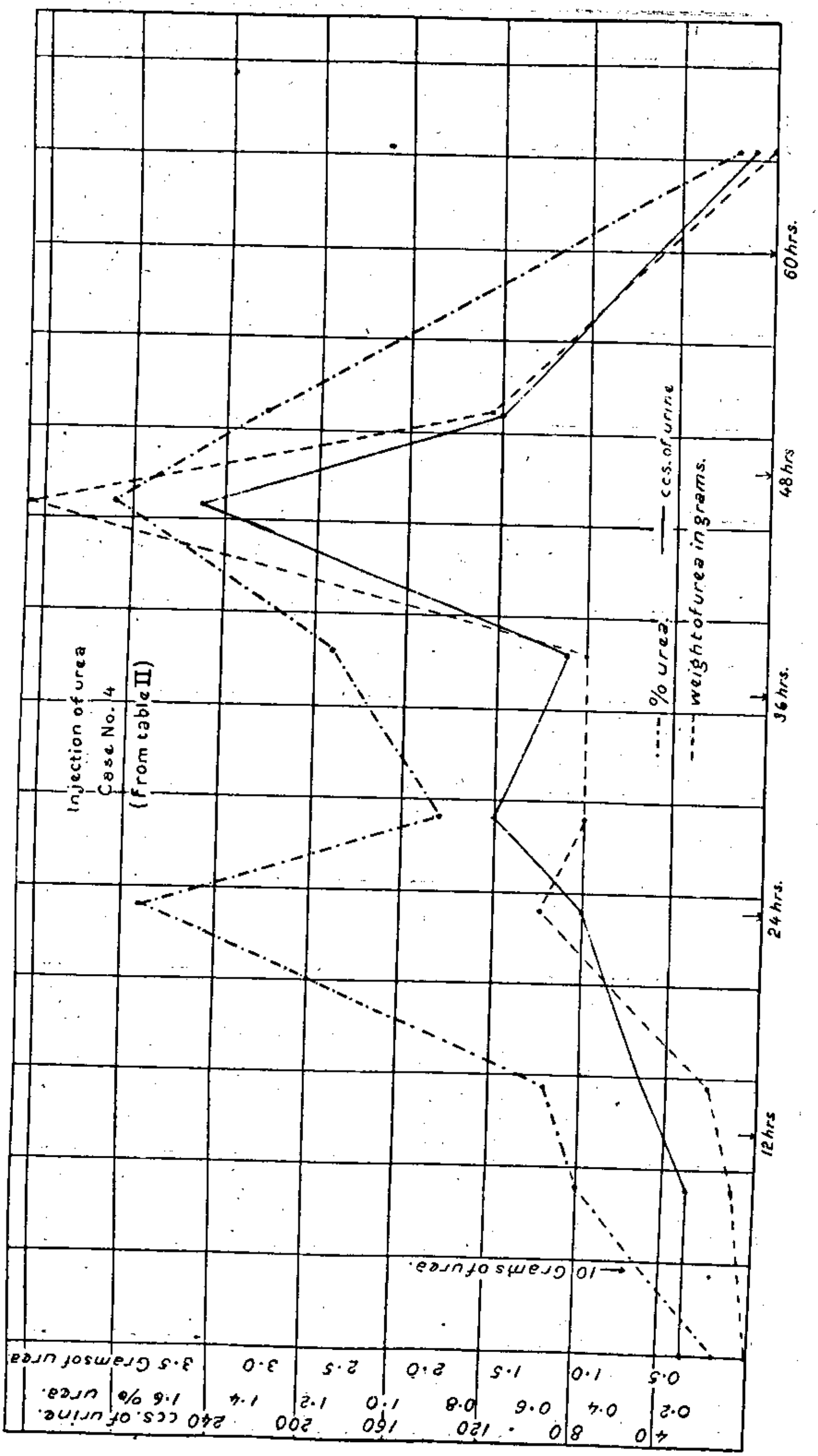
There is some evidence which indicates that the suppression of urea is not due to an impairment of function in the urea-forming organs. It was found in patients who were excreting only minimal amounts of urine that on the administration of bicarbonates the urea content sometimes rose almost to normal within a comparatively few hours. Thus, in one case, the percentage of urea rose from 0.05 per cent to 1.3 per cent in five hours. The data for this case are given in Table VI.

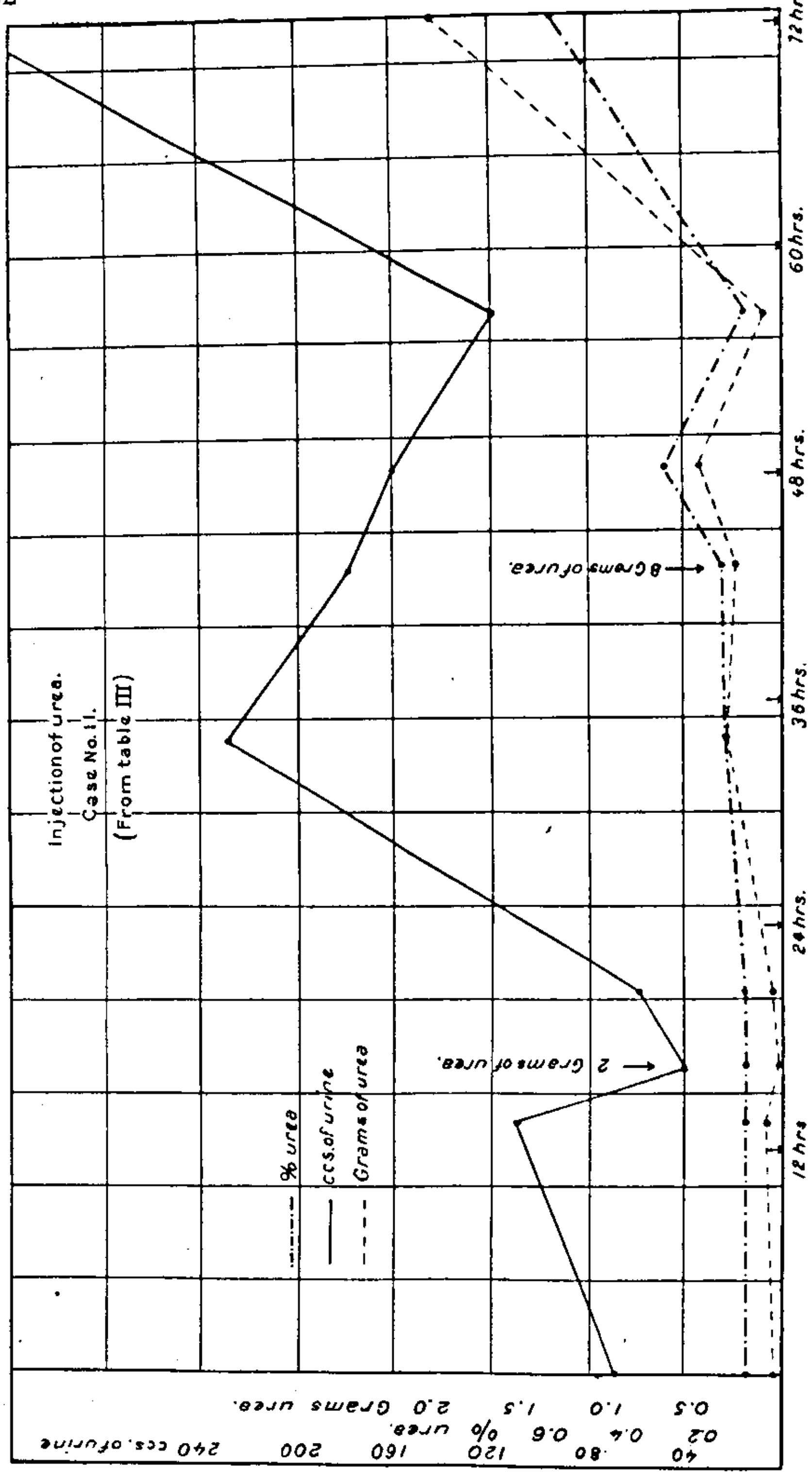
TABLE VI.—*Injection of sodium bicarbonate.*

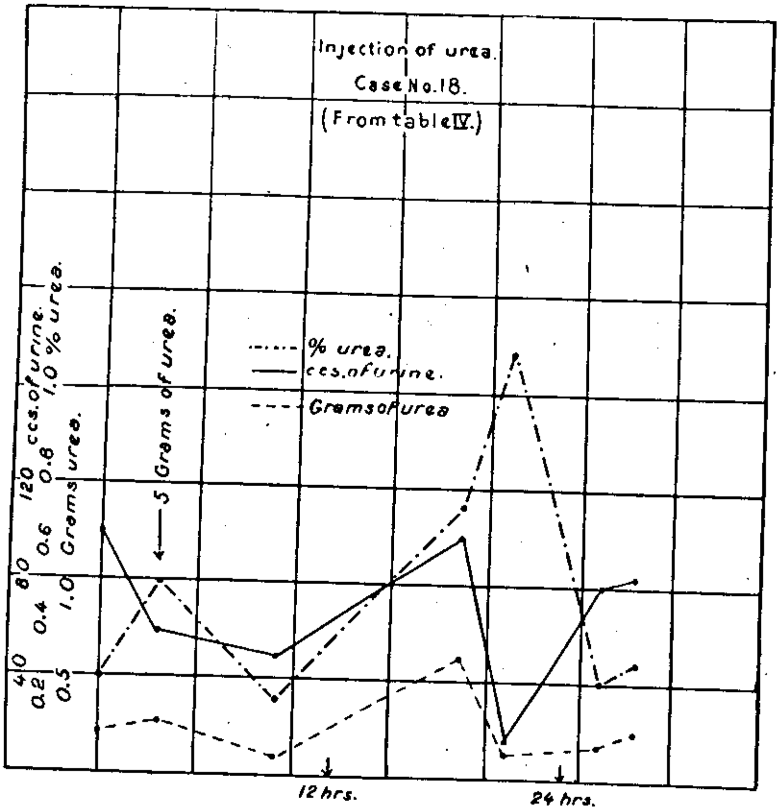
Interval between specimens.	Cubic centimeters of urine.	Per cent of urea.	Grams of urea.
Hours.			
---------	15	0.05	0.0075
6¼	6	0.05	0.003
8	2	0.05	0.001
Injection of 30 grams sodium bicarbonate.			
4	300	0.05	0.15
2¼	110	0.5	0.55
1	150	0.8	1.2
1¼	220	1.3	2.86
3	200	1.5	3.00
4	240	1.2	2.88
Recovery.			

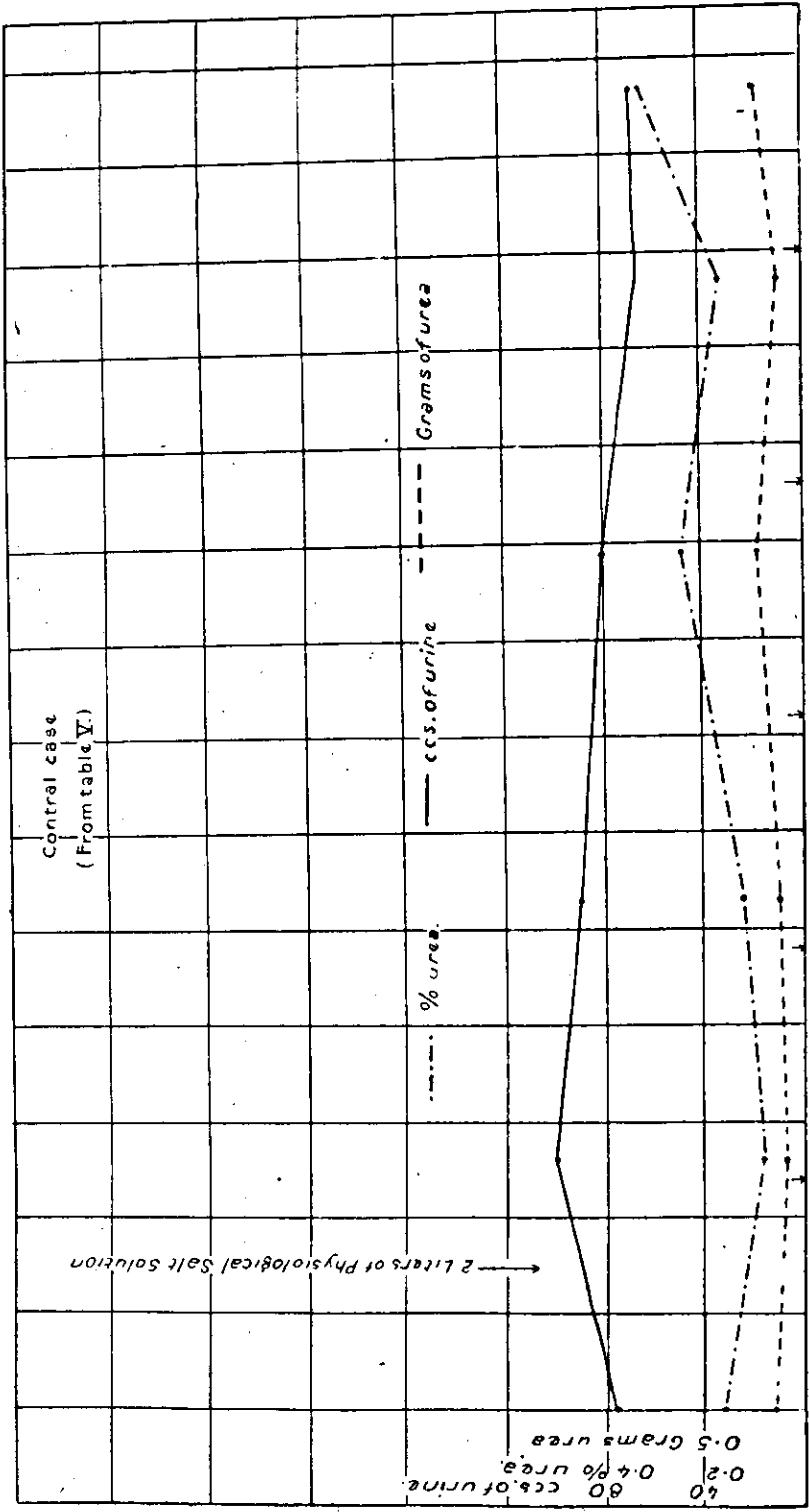
This might be interpreted as indicating that until the alkali was injected, nitrogenous material was being utilized for the neutralization of acids. However, there is one step in this explanation which is not clear. If the nitrogen neutralizes acids, one would expect to find ammonium salts in the urine on testing with sodium hypobromite, unless the neutralization took place in such a way that the resulting product failed to be excreted in the urine, or perhaps failed to react with the evolution of gas in the presence of the hypobromite.

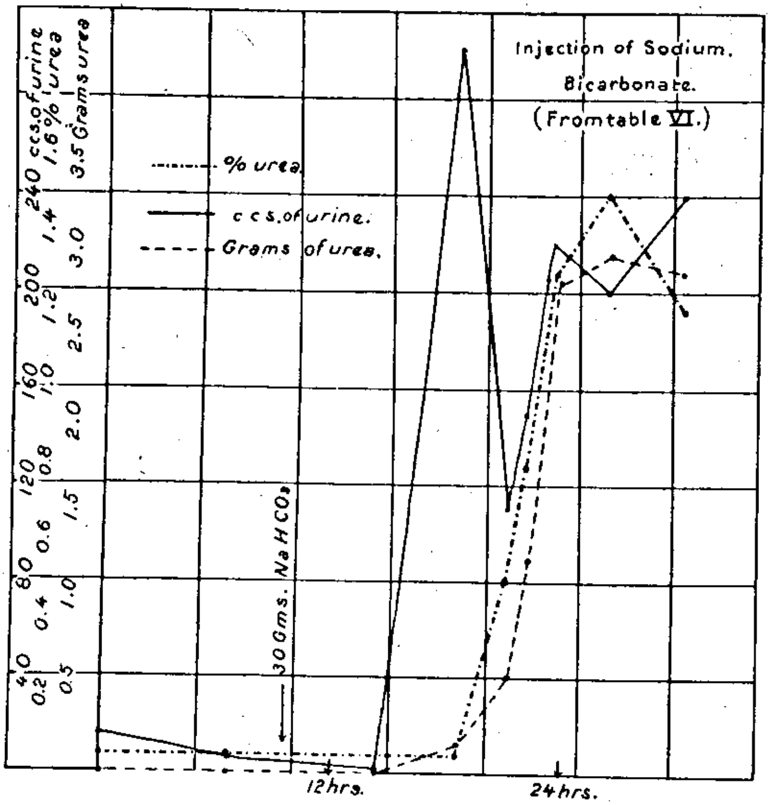
For convenience, the results of the injections of urea and of sodium bicarbonate have been plotted in the accompanying charts. One of the urea cases (number 15) has been omitted as the data were incomplete. In two cases (numbers 11 and 18), the specimens of urine which were necessary for quantitative results could not be obtained; the qualitative changes, although somewhat suggestive, are not conclusive. The chart from Table II (case number 4) is especially interesting. Here the urea content following the injection of urea, rises from 0.1 to 1.8 per cent and then returns rapidly to its original point. The chart corresponding to Table VI gives the effect of the injection of sodium bicarbonate. Here the urea content rises from almost zero to normal and continues a normal course. In the control case, the amount and per cent of urea remain constantly low.


Injection of urea
Case No. 4
(From table II)
ccs. of urine
% urea.
weight of urea in grams.
10 Grams of urea.
12 hrs
24 hrs.
36 hrs.
48 hrs
60 hrs.
0.5 1.0 1.5 2.0 2.5 3.0 3.5 Grams of urea
0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 % urea.
40 80 120 160 200 240 ccs. of urine.


Injection of urea.
Case No. 11.
(From table III)
% urea
ccs. of urine
Grams of urea
2 Grams of urea.
8 Grams of urea.
12 hrs
24 hrs.
36 hrs.
48 hrs.
60 hrs.
72 hrs.
0.5 1.0 1.5 2.0 Grams urea.
0.2 0.4 0.6 % urea.
40 80 120 160 200 240 ccs. of urine


Injection of urea.
Case No. 18.
(From table IV.)
% urea.
ccs. of urine.
Grams of urea
ccs. of urine.
% urea.
Grams urea.
120
80
40
1.0
0.8
0.6
0.4
0.2
1.0
0.5
← 5 Grams of urea.
12 hrs.
24 hrs.


Contral case
(From table V.)
ccs. of urine
Grams of urea
% urea
60 hrs
48 hrs
36 hrs
24 hrs
12 hrs
2 Liters of Physiological Salt Solution
40 80 ccs. of urine.
0.2 0.4 % urea.
0.5 Grams urea



Carbon dioxide content of the blood.—In view of the decreased alkalinity of the blood which has been reported in cholera, it would naturally be of interest to determine its carbon dioxide content. In selecting a method for carbon dioxide determinations of the blood it must be remembered that none of the various procedures are free from error. The gravimetric method was used in the following determinations, according to the technique of Kraus.(4)

Blood was withdrawn with an ordinary syringe from a superficial vein of the arm below an Esmarch bandage and defibrinated with glass beads in a closed flask. The pressure throughout the apparatus was reduced to 16 centimeters. Approximately three to four times the theoretical amount of sulphuric acid was added using a 1 per cent solution instead of the more concentrated acid recommended by Kraus. After the addition of the acid, the apparatus was washed with air under the reduced pressure until the weight of the absorption bulbs was constant. Two absorption bulbs for carbon dioxide were used in order that the process might be carried out rapidly. The entire procedure was usually completed within three hours.

No determinations were made upon cases in collapse or in the stage of reaction, but only on those in which symptoms of uræmia were present. Two patients were available.

Case number 15 was tested on the fourth day of the disease, two hours before death. A total of 50 cubic centimeters of urine were excreted during the course of the illness. There were moderate symptoms of uræmia, and a typhoidal condition was also present. Case number 18 was tested on the third day of the disease, twenty hours before death. A total of 500 cubic centimeters of urine were excreted during the four days. There was only slight elevation of the blood pressure. The respirations were deep but the rate was not increased.

Determinations with this method on normal human blood gave results which closely approximated those obtained by volumetric methods, namely 40 to 50 volumes per cent of carbon dioxide. The specific gravity of normal blood (1.060) was used in calculating the volume of the sample of cholera blood from its weight. It is evident that this determination can represent only an approximation. However, the tendency of the error would lie in the direction of a high result rather than a low one. There was little opportunity for loss of carbon dioxide, but considerable care was required to prevent water from being carried over into the absorption bulbs. In these two patients there does not seem to be any reasonable doubt but that the carbon dioxide of the blood was definitely reduced below the normal.

TABLE VIII.—*Carbon dioxide content of the blood.*

Sample.	Weight of blood.	Increase in weight in CO_2—absorption bulbs.		Total carbon dioxide.	Volume per cent of carbon dioxide.
		I.	II.		
Blank with water:	*Grams.*	*Grams.*	*Grams.*	*Grams.*	
I.		0.0009			
II.		0.0017			
Normal individuals:					
A	15.10	0.0144	0.0003	0.0147	51
B	17.47	0.0110	0.0023	0.0133	40
Cholera patients:					
No. 15	17.125	0.0062	0.0023	0.0085	26
No. 18	27.66	0.0065	0.0018	0.0083	16

In connection with these carbon dioxide determinations of the blood, it is interesting to note that Wittstock(5) has reported a decrease in the absorption of oxygen by the lungs and a decreased output of carbon dioxide in cholera.

EFFECT OF ALKALINE SOLUTIONS.

The results of alkaline therapy in diabetes have been of some value in the study of acid intoxication. Perhaps the simplest interpretation of these results is that, although an excessive amount of acid is usually present, yet it is probably not the sole ætiologic factor in the production of coma. The conditions in cholera in some respects are unusually favorable for observing the action of alkalies. For the most part, the patients are obtained after only a few hours of illness and before any symptoms of acid intoxication are present.

It has already been found that alkalies in large quantities produce a prompt excretion of urine in the stage of reaction. The most desirable period at which to commence the injection of alkalies and the most suitable concentrations were not definitely determined and therefore these questions have been given especial consideration in the following group of cases. In the main, two procedures suggest themselves. An apparently satisfactory plan would consist in the use of salt solution during the stage of collapse, followed by alkali in case the anuria persists during the stage of reaction. This has the disadvantage of requiring a considerable increase in the amount of fluid injected. For example, a patient receiving 5 to 10 liters of salt solution during the first day of collapse may require perhaps an additional five liters of alkali to start the excretion of urine. There are also certain theoretical objections to delaying the injection of alkali until the tolerance toward it has become well established. Such a delay would tend to favor the production of ammonium salts in the body. The toxicity of these salts in acid intoxication has been suggested by Mendel(6) and by Carlson and Jacobson.(7) Furthermore, if acids are allowed to accumulate, they may produce a permanent injury to the tissues which can not be remedied by the removal of the acids by neutralization. This suggestion has been offered in explanation of the merely temporary improvement after the use of alkalies in diabetic coma. A somewhat analogous condition may occur in cholera. It was noted in the uræmic stage, that the late administration of alkalies would cause a prompt excretion of urine and apparently prolong life for several days, although death ultimately took place. The free diuresis, following the bicarbonate injections when the stage of reaction appears, would afford better opportunities for elimination than could be effected by the intestinal tract alone.

However, during the stage of collapse when many liters of fluid are being lost by rectum no measures whatever have been effectual in producing excretion of urine. It is also a fact that the use of alkali during collapse has given no definite indication that it possesses any advantage over a neutral solution. Indeed the higher concentrations of 1 and 2 per cent can only be used for the first injection in carefully selected cases.

The following patients were treated with alkali with the object of determining the maximum concentration of sodium bicarbonate which could be used during collapse as a routine for all cases. Although a previous series showed that a fatal uræmia did not develop after large amounts of alkali, yet it is important to know definitely whether there is any increase in the number of deaths from other causes, that is, to know that patients who would have died in uræmia were not merely dying in collapse under alkaline treatment before the uræmic stage was reached. The possibility also has been suggested that uræmia causes only an apparent increase in the mortality, namely, that those cases which die in uræmia would terminate fatally from other causes if the course of the disease were not shortened by uræmia.

The patients available for this investigation were received at the hospital in the majority of instances rather early in the course of the disease only about one-half being in complete collapse. Several conditions indicate that the epidemic was at least moderately severe. During the period of investigation there were sixty-five deaths among untreated cases remaining in their homes, although the number of recoveries under such conditions is not available. There were a few individuals who died immediately on arrival at the hospital, or at the commencement of the first intravenous injection; two patients were received in an almost moribund condition and others repeatedly went into collapse, notwithstanding the frequent injection of salt solution. The disease in all instances was diagnosed bacteriologically by the staff of the Bureau of Science, the cholera vibrio being isolated in pure culture from the fæces and identified by agglutination reactions. Only uncomplicated cases showing typical clinical symptoms were selected; those presenting serious complications in addition to the cholera infection were not included. Thus, one case, admitted in pregnancy at full term, is omitted from the series, as well as another in which there was extensive tuberculosis. On admission to the hospital, the patients were divided into two groups of which one received the ordinary saline treatment and the other a solution containing 0.5 per cent of sodium bicarbonate. In the stage of reaction, the concentration of the bicarbonate was increased to 1.5 per cent in those cases in which suppression of urine persisted. As a routine the solutions were injected intravenously in 2-liter quantities, during the course of fifteen to thirty minutes. In the stage of collapse, 4 liters of fluid were occasionally required for the first injection while in the stage of reaction 1 liter of 1.5 per cent sodium bicarbonate was sometimes sufficient.

PREPARATION OF RINGER-LOCKE AND OF THE ALKALINE SOLUTION.

For the control series an isotonic Ringer-Locke solution was prepared according to the formula: sodium chloride 0.9 per cent, potassium chloride 0.042 per cent, calcium chloride, crystallized, 0.024 per cent and sodium bicarbonate 0.03 per cent.

The sodium bicarbonate was added to determine whether these salts in the proportions in which they normally occur in the blood might not produce an effect similar to that obtained with larger amounts of the bicarbonate alone.

A solution of the preceding formula can not be sterilized by heat without conversion of the bicarbonate to the normal carbonate followed by subsequent precipitation of the calcium. Consequently the first three salts were added and the solution heated in the autoclave. The required amount of sodium bicarbonate was added in solid form immediately before the injection of the solution.

The formula was modified as follows for the alkaline injections during collapse: Sodium chloride 0.4 per cent, potassium chloride 0.042 per cent and sodium bicarbonate 0.5 per cent. The calcium was omitted on account of the insolubility of its carbonate. When the 0.024 per cent of calcium chloride was added in the presence of the 0.5 per cent of bicarbonate, a supersaturated solution occasionally would be obtained which would remain clear for a short period, but precipitation usually occurred after 20 to 30 minutes. An attempt was made to prepare the solution of sodium bicarbonate with a minimal conversion to the normal carbonate. The injection of sodium bicarbonate in aqueous solutions entirely free from normal carbonate would appear to be impossible since even at room temperature conversion to the normal carbonate takes place. Thus McCoy(8) found that in tenth molecular aqueous solutions at 25° C., 2.68 per cent of the bicarbonate immediately was converted to the normal carbonate and that equilibrium was not established until only 40 per cent of the bicarbonate remained unchanged. In stronger solutions the decomposition was much more rapid, e. g., in three-tenths molecular solutions, 77 per cent, and in molecular solutions, 86.2 per cent of the bicarbonate was decomposed at once. In view of these changes, the 0.5 per cent of bicarbonate was added in solid form to the sterilized solutions containing the sodium and potassium salts and the injection was made immediately without further heating of the solution. Samples of freshly prepared sodium bicarbonate were selected which were shown to be sterile when tested on ordinary culture media.

The 1.5 per cent bicarbonate solutions for injection during the stage of reaction were prepared without the addition of any other salt and were heated in the autoclave at 3 kilograms pressure per square centimeter for forty-five minutes, about 25 per cent of the bicarbonate being converted to the normal carbonate, under these conditions. For the preparation of 0.5 per cent bicarbonate solutions on a larger scale, it was found that an average decomposition of less than 3 per cent occurred when the solutions were heated in the autoclave in tightly stoppered bottles at a pressure of 3 kilograms per square centimeter for forty-five minutes, allowing the autoclave to cool to room temperature before opening to the atmosphere. The amount of normal carbonate in the solutions after sterilization was determined by titration at 0°C., against $\frac{N}{100}$ hydrochloric acid in the presence of phenolphthalein. The solutions were titrated within four days after sterilization. In two separate lots of solutions, the variations from this mean of 3 per cent were only slight. This amount of change is not greatly in excess of the conversion which takes place in the corresponding unheated solutions.

This solution was subsequently tested upon three typical cases in collapse and all recovered. The response from collapse was quite similar to that obtained with ordinary physiological saline solution. These three patients were sporadic cases occurring late in the cholera season, and for this reason they are not included in the group which is reported later.

Another factor was introduced in that some of the severest cases also received an anticholera serum. The reports concerning anticholera sera indicate on the whole that there is a certain minimal benefit to be derived from its use.(9, 10, 11) Its effect on the death rate is not sufficiently great to constitute any conclusive evidence of its value. Furthermore, if the use of alkalies affects only those cases which die in uræmia (15 per cent), then its influence on the death rate would not be very pronounced. By utilizing both methods of treatment it was thought that the combined effect might be great enough to show itself.

Aside from its having antitoxic properties, the serum perhaps might be of some minor value in protecting the corpuscles and the proteins of the blood from the action of the alkali; also it might aid in the retention of the injected fluid within the blood vessels, especially if the exudation of fluid through the vessel walls is dependent upon vital as well as physical phenomena.

The serum was prepared in a manner somewhat similar to that followed by Schurupoff.(10) Ten strains of cholera vibrios were tested and no marked differences were found in the minimal lethal dose of the killed cultures upon intraperitoneal injection into guinea pigs. The cultures were killed by adding sodium hydroxide to a thick emulsion of cholera vibrios in physiological saline solution.

Only freshly isolated strains of cholera were employed for the preparation of the serum, a new strain being obtained every month. The growth from 15 to 20 large agar slants was used for each injection, the slants each measuring about 3 by 8 centimeters. This growth was suspended in 20 to 30 cubic centimeters of salt solution and for the first injection the vibrios were killed by the addition of 2 cubic centimeters of $\frac{N}{1}$ sodium hydroxide. Upon the addition of the alkali, the suspension changed from a limpid, opaque emulsion to a viscous, translucent solution. The viscosity was so great that dilution with an equal volume of salt solution was usually required in order to effect a thorough mixing. Further addition of the hydroxide diminished the viscosity of the fluid and apparently rendered it less toxic. The amount of sodium hydroxide was gradually decreased, until toward the end of the period of immunization, only one-fourth of original amount was used. This was not sufficient to kill the emulsion of vibrios, but their virulence for guinea pigs was diminished.

The injections were made intramuscularly at intervals of about two weeks over a period of four and a half months. Determinations were made of the protective power of the serum for guinea pigs against intraperitoneal inoculation of the vibrio emulsion killed with sodium hydroxide. The serum was tested before the injections were begun and at the end of the period of immunization, but no definite increase in this protective power could be detected. Three to 5 cubic centimeters of horse serum, either before or after treatment of the animal, when digested for thirty minutes with the minimal lethal dose of the cholera suspension (usually 1 to 2 cubic centimeters for intraperitoneal injection) were sufficient to completely protect guinea pigs of 300 grams. Sera of much higher efficiency have been obtained, notably that of Salimbeni(12) 0.002 cubic centimeter of which neutralized twice the lethal dose of cholera toxin. The behavior of the horse itself showed little evidence of immunity. The subcutaneous injections produced a local swelling and some rise in temperature. As the injections were continued there was only a slight diminution in this reaction. Finally, the minimal lethal dose by intravenous injection of the killed cholera material was determined upon normal horses. Three months after the last subcutaneous injection and after the horse had been under treatment for nine months, the intravenous injection of the minimal lethal dose, about 4 cubic centimeters, produced a fatal result in twelve hours.

The serum was used intravenously in 200 cubic centimeter quantities in 1 to 10 dilution in 0.5 per cent sodium bicarbonate solution. No more than two injections were made in any given case; therefore the maximum amount of the anticholera serum for any patient was 400 cubic centimeters. Favorable results have been reported with larger amounts, such as 1,040 to 1,390 cubic centimeters.(10) A very limited number of cases were treated with serum. Only those patients were selected in which the general symptoms were severe and the state of collapse was extreme. Six of these cases in the bicarbonate series were of this type. Two died in collapse without any definite response to the injections. The four remaining recovered, but without any pronounced differences from extreme cases which recover under sodium chloride treatment. However, the recovery of four of these six patients was unexpected and a control series with normal serum seemed advisable, but practically no cases were available. Only one patient was tested. He was admitted in complete collapse, and the toxæmia, though well marked, was not extreme. In all 600 cubic centimeters of normal horse serum were injected and a total of 12 liters of fluid. There was only a slight response to the injections. On the third day there were three moderately large hæmorrhages from the bowel, and death occurred on the fourth day.

Autopsy showed extensive œdema of the left lung with adhesions of the pleura. Multiple hæmorrhagic infiltrations extending to the serous coat were found in the small intestine. These areas measured about 1 centimeter in diameter; they were most numerous just above the ileo caecal valve and gradually disappeared in the upper fourth of the intestine.

The results, with the two groups of cases, showed that with Ringer's solution, only a small percentage of cases recovered after more than one day of anuria. In the bicarbonate group, a number recovered after one day of complete suppression of urine. The data are as follows:

Treatment.	Duration of anuria.	
	Less than 24 hours.	24 to 48 hours.
Ringer's	10	3
Bicarbonate	10	8

In dividing the patients into two similar groups, both the severity of the cholera symptoms and the general physical condition of the patients were considered. As nearly as could be determined there was no difference in either direction in the severity of the two series. The group treated with serum and bicarbonate represents those cases which went into complete collapse and in whom the symptoms of toxæmia were more or less prominent. Of the fifteen individuals treated with bicarbonate alone, five, and of the twenty-two control cases, twelve, were admitted in complete collapse.

The following classification has been used for estimating the effect of the bicarbonate solutions on the cause of death. Under collapse and enteritis are included those cases which die primarily from loss of fluid and also those which continue to live until the enteritis with its accompanying toxæmia is well developed. The uræmia of cholera, while differing from that of ordinary nephritis, is nevertheless characteristic. Two cases occurred in which symptoms both of uræmia and of the toxæmia of the cholera infection were present. Since each of these conditions may have been contributing factors in the cause of death, these are recorded as "intermediate."

The final results are given in the accompanying outline.

Treatment.	Number of cases.	Cause of death.			Total number of deaths.	Total number of recoveries.[a]
		Collapse.	Uræmia.	Intermediate cases.		
Bicarbonate and serum[a]	7	3			3	4
Bicarbonate	15	1			1	14
Total with bicarbonate	22	4			4	18
Control with Ringer's	22	5	2	2	9	13

[a] Including one patient receiving normal serum.

The patient who died under treatment with bicarbonate alone was a child eleven years old admitted in partial collapse.

Although in the control series there were only four deaths in which symptoms of uræmia were present, yet because of the constancy of uræmia, its absence is suggestive in the group of cases treated with bicarbonate and serum. Theoretically, the serum might prevent the development of uræmia if it could abort the infection.

There was no evidence to indicate that the serum was responsible for the absence of uræmia. In large epidemics where serum has been used extensively, nothing has been reported to show that the incidence of uræmia is lessened. The number of cases, treated without serum, namely fifteen, represent those which were less severe; but since even the mild cases are not always free from uræmia, this group would suggest that it was not the serum which prevented the development of this complication.

One patient (number 10), in the bicarbonate series, developed symptoms of uræmia. This case was admitted in complete collapse and responded poorly both to the injections of fluid and also to the serum, 200 cubic centimeters of which were used. During the first eighteen hours, 6 liters of 0.5 per cent bicarbonate were injected. At the end of the first day, during which time only 15 cubic centimeters of urine were obtained, the concentration of the sodium bicarbonate was increased, 1 liter of a 1.5 per cent solution being injected. Eight hours later, 140 cubic centimeters of urine were obtained by catheter, but this rate of excretion soon diminished and after nine hours an additional 15 grams of bicarbonate in 1 liter of water were given intravenously. After a twelve-hour interval only 70 cubic centimeters of urine were secured. The patient was not clear mentally, the restlessness was increasing, and the general condition was not good. A sixth injection of bicarbonate was given consisting of 2 liters of a 1.5 per cent solution.

As soon as the injection was well started, the patient complained severely of pain throughout the body and of cramps in the muscles. After the administration of one liter, there was considerable contraction and twitching of the muscles, which was especially noticeable in the extremities. The rigidity of the muscles did not entirely pass away until after eight hours. This is the only case in the series which developed muscular twitchings. A specimen of blood taken at that time showed a trace of hæmolysis, although none was observed after the use of 1.5 per cent sodium bicarbonate in a number of other cases. At this time, eight hours after the injection, no urine had been obtained and the symptoms of uræmia persisted. In view of the pronounced reaction which had followed the last injection it did not seem advisable to continue the injections of alkali. This case had received a total of 90 grams of sodium bicarbonate in two days. The patient had certainly passed the stage of collapse and as the anuria had not yielded to the injections of alkali, it apparently constituted a definite exception to the other cases. However, after an additional four hours 120 cubic centimeters of urine were obtained by catheter, and in the next twenty-four hours 1,200 cubic centimeters. The mental condition rapidly returned to normal after the excretion of urine commenced.

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A STATISTICAL STUDY OF INTESTINAL PARASITES IN TOBACCO HACIENDAS OF THE CAGAYAN VALLEY, PHILIPPINE ISLANDS.*

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TABLE I.—*Summary of findings.*

Examinations and infections.	Number.	Per cent.
Persons examined	4,278	
Persons infected	3,656	85.46
Persons infected with—		
Ascaris	2,653	62.04
Hookworm	2,326	54.37
Trichuris	342	7.99
Oxyuris	64	1.50
Tænia	59	1.38
Hymenolepis	5	0.12
Strongyloides	4	0.09
Trematodes[a]	1	0.02
Total infections	5,454	127.49

[a] Probably *Fascioletta ilocana* Garrison, 1908.

Upon the completion of the medical survey of the town of Taytay,[1] Rizal Province, in 1909, which was an effort to determine the health conditions in a representative Filipino community and which included the examination of the fæces of 1,000 persons, the Bureau of Health inaugurated a campaign to determine the frequency and medical importance of intestinal parasitism in other parts of the Island of Luzon with particular reference to the incidence and significance of hookworm infections. During the survey, 6,018 persons were examined at Las Piñas, Rizal Province; 2,594 at Tuguegarao, Cagayan Province; 802 at Santa Isabel, 3,310 at San Antonio, and 968 at Maluno, barrios of Ilagan, Isabela Province. The results obtained at the first three places have already been reported.[2] The present paper contains the findings at the last two places named.

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* Read at a meeting of the Manila Medical Society, January 9, 1911.

[1] *This Journal, Sec. B* (1909), 4, 207.

[2] Rissler and Gomez, *This Journal, Sec. B* (1910), 5, 267.

San Antonio and Maluno are tobacco haciendas. At the former place, 74.25 per cent of the population was examined; at the latter, 93.44 per cent. Therefore, the percentages of the various parasites found may be accepted as representing those present in the general population of the two haciendas.

In order that the work of the haciendas might not be too greatly interrupted at a time when there was a great deal to do in the fields, it was necessary to allow the people to save the specimens overnight; hence, the great majority of these were unfavorable for examination for the presence of amœbæ and flagellates, and no systematic search was made for the latter two classes of organisms. However, very few infections with these parasites were seen, so that it is believed they are infrequent at these two haciendas. The findings of Rissler and Gomez[3] in the Cagayan Valley are in accord with this impression and only one case of marked dysentery was seen; this probably was not amœbic since it responded to bismuth.

Nearly all of the persons examined were Ilocanos who migrated into the Cagayan Valley. There are included in the list the Spanish officials of the haciendas, 83 Ibanags composing *cabeceria* number 9, and 58 Visayans composing *cabeceria* number 33, of San Antonio. The findings among the Ibanags did not differ essentially from those among the Ilocanos, whereas the Visayans showed a high percentage of infection with the hookworm (77.59 per cent) and the whipworm (63.79 per cent).

Each hacienda is divided into districts which are subdivided into *cabecerias*. There are thirty-three such *cabecerias* at San Antonio and twelve at Maluno. Most of the houses are located on hills which are rocky, but which usually have a few trees. It appears that the selection of such sites for homes accomplishes a double purpose: It gives the tenants the advantage of available shade and places them above the water mark when the lowlands are flooded at various times during the rainy season. However, some of the houses are located in the lowlands. The variation in the location of the houses in the different *cabecerias* plays a rôle in the occurrence of the hookworm.

Several factors are acting upon the persons examined, excepting the officials, to lower their general vitality and render complex the problem of determining the effect upon them of intestinal parasitism. Marriage occurs early; child bearing is rapid; smoking is commenced at a tender age and is indulged in excessively throughout life; drinking of native whisky is commenced early; the diet is poor and consists of rice and maize, largely maize, with very little meat; and tuberculosis is common. Fortunately, malaria is rare.

The results obtained are based upon the examination of two thin coverslip preparations of each specimen; it is understood that the findings of

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[3] *Loc. cit.*

Rissler and Gomez were from the examination of one cover-slip preparation of each case. However, my results may be compared with theirs according to the testimony of a Filipino boy who made many of the preparations at Las Piñas, a large number of the microscopic examinations at Tuguegarao and Santa Isabel, and practically all of my own preparations, since no more fæcal material was used in two of my preparations than in one of Rissler and Gomez.

RESULTS COMPARED WITH OTHER STATISTICAL STUDIES IN THE PHILIPPINES.

The results obtained are compared in Tables II and III, respectively, with those in other parts of the Philippines as to the number of infections found and the various parasites present.

TABLE II.—*Percentages of persons infected and total infections in various parts of Luzon.*

Authority and date.	Place.	Sex.	Examined.	Infected.	Per cent.	Total infections.[b]	Per cent.
Garrison,[4] 1908	Manila	Mostly males	4,106	[a]3,447	84.00	5,812	142.00
Garrison and Llamas,[5] 1909.	do	Women and children.	385	[b]342	89.00	533	138.70
Garrison, Leynes and Llamas,[6] 1909.	Taytay, Rizal	Males and females.	1,000	[a]959	95.90	1,726	172.60
Rissler and Gomez, 1910.	Las Piñas, Rizal	do	6,018	[a]5,406	89.83	8,996	149.48
Do	Tuguegarao, Cagayan.	do	2,594	[a]1,932	74.13	2,887	111.30
Do	Santa Isabel, Ilagan, Isabela.	do	802	[a]692	86.28	927	114.34
Chamberlain, Bloombergh and Kilbourne,[7] 1911.	Baguio, Benguet	Adult males	119	[b]110	92.50	209	174.00
Willets, 1911	San Antonio and Maluno, Ilagan, Isabela.	Males and females.	4,278	[b]3,656	85.46	5,454	127.49
Total			19,302	16,535	85.66	26,544	137.52

[a] Protozoan findings included.

[b] Intestinal worms only.

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[4] *This Journal, Sec. B* (1908), 3, 191.

[5] *Ibid.* (1909), 4, 185.

[6] *Ibid.* (1909), 4, 207.

[7] *Ibid.* (1910), 5, 505.

TABLE III.—*Comparison of the various parasites reported in different parts of Luzon.*

Authority.	Date.	Place.	Number examined.	*Ascaris.*		*Trichuris.*		Hookworm.		*Oxyuris.*		*Strongyloides.*		*Tænia.*		*Hymenolepis.*	
				Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Garrison	1908	Manila, Bilibid Prison	4,106	1,052	26.00	2,426	59.00	2,135	52.00	32	0.80	132	3.00	30	0.70	5	0.10
Garrison and Llamas.	1909	Manila, hospitals, etc	385	182	53.22	300	87.60	46	13.45	2	0.60	2	0.60	1	0.30	0	0.00
Garrison, Leynes and Llamas.	1909	Taytay, Rizal Province	1,000	829	82.90	770	77.00	116	11.60	4	0.04	7	0.70	0	0.00	0	0.00
Rissler and Gomez.	1910	Las Piñas, Rizal Province.	6,018	4,647	77.21	3,241	53.40	671	11.14	298	4.95	135	2.24	4	0.06	0	0.00
Do	1910	Tuguegarao, Cagayan	2.594	1,907	73.55	672	25.90	208	8.01	68	2.62	0	0.00	13	0.50	19	0.73
Do	1910	Santa Isabel, Ilagan, Isabela.	802	486	60.59	50	6.23	364	45.38	10	1.24	0	0.00	11	1.37	6	0.74
Chamberlain, Bloombergh and Kilbourne.	1911	Baguio, Benguet	119	87	73.00	72	60.00	35	29.00	0	0.00	0	0.00	15	12.00	0	0.00
Willets	1911	San Antonio and Maluno, Ilagan, Isabela.	4,258	2,653	62.04	342	7.99	2,326	54.37	64	1.50	4	0.09	59	1.38	5	0.12
Total			19,302	11,843	61.36	7,873	40.79	5,901	30.57	478	2.48	280	1.45	133	0.69	35	0.18

In some of the studies the number of persons infected with intestinal worms alone is not stated as indicated in the table. It is probable that the findings at San Antonio and Maluno do not differ essentially from those in other parts of Luzon, excepting Tuguegarao, where approximately 10 per cent less of the population were infected than elsewhere.

It is noteworthy that the number of infections with intestinal worms per 100 persons examined was decidedly lower in the Cagayan Valley than in other parts of the island; this probably is due to the relatively low percentages of whipworm infections encountered in that locality.

The striking features of the findings at San Antonio and Maluno are the high percentage of persons infected with the hookworm and the low percentage with the whipworm (*Trichuris*). Rissler and Gomez found 45.38 per cent of the 802 individuals and 60.58 per cent of the adult males examined at Santa Isabel (which is also a tobacco hacienda) infected with the hookworm whereas 54.37 per cent of the 4,278 persons and 74.89 per cent of the adult males composing the present series harbored the parasite. That is, 8.99 per cent more of the general population and 14.31 per cent more of the adult male population was infected with the hookworm than heretofore reported for any section of the Philippine Islands. Garrison's series of 4,106 cases examined at Bilibid prison and which gave 52.00 per cent of hookworm infection, was composed almost entirely of adult males.

In my opinion, three factors are acting to produce a high percentage of hookworm infection at the haciendas, namely, the nature of the soil, the tobacco plants, and the occupation of the people. The soil is composed of clay with which sand is generously admixed, the tobacco plants furnish shade-conditions which are favorable for the propagation of the hookworm, and the cultivation of the tobacco keeps the people in the field daily during the greater part of the year. The belief that the infections are obtained in the fields is supported by the facts that the hookworm percentage increases rapidly when the age is reached at which work in the fields is begun,[8] that males, who are in the fields more than females, give a higher percentage of infection than the females, and that a greater percentage of persons are infected in the lowlands than in the uplands.

The findings in regard to the whipworm were quite as unexpected as those for the hookworm. Prior to the work in the Cagayan Valley, statistical studies had shown *Trichuris* to be very common in the Philippine Islands, Garrison and Llamas finding as high as 87.60 per cent of 385 women and children of Manila infected with it. Rissler and Gomez found 25.90 per cent of the persons examined at Tuguegarao and 6.23 per cent of those examined at Santa Isabel to be infected with the same parasite. (See Table III.) At Maluno only 4.75 per cent and at San Antonio 8.94 per cent of those examined harbored the whipworm. At the latter place the percentage was raised because of the presence of some Visayans who had been in the valley about one year and many of whom were infected with the parasite in question and because the inhabitants of certain *cabecerias* made frequent visits in Ilagan *Central.*

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[8] That is, about 7 years.

The low percentage of whipworm infection probably is due to a lack of introduction of this parasite in great numbers in the haciendas. *Trichuris* and *Ascaris* have thick-shelled ova and high percentages of these parasites are not infrequently found in a given community. The conditions favorable for the propagation of the one are, in a general way, favorable for the other. Now, the round worm is the parasite which occurs most frequently at the two haciendas. That the lack of introduction in sufficiently great numbers accounts for the relative infrequency of the whipworm is supported further by the fact that the neighbors of the Visayans to whom reference has been made and persons living near Ilagan *Central* show a higher percentage of infection with this parasite than do those who live at a distance.

Trematode ova in the stool of a boy 13 years of age appeared to be those of *Fascioletta ilocana* Garrison. Other than this, no unusual infection was seen.

COMPARISON OF FINDINGS AT SAN ANTONIO AND MALUNO.

Practically all of the people at the haciendas are of the same origin, and since they are all engaged in the same sort of labor in the same kind of soil it was to be expected that there would be but slight variations in the findings at the two places. This proved to be true.

Table IV shows the percentage of persons at the two haciendas who harbored single, double, triple, and quadruple infections and also the number per 100 persons examined. The great majority of the single infections was with the hookworm, or *Ascaris;* of the double, hookworm and *Ascaris;* and of the triple, hookworm, *Ascaris* and *Trichuris.*

TABLE IV.—*Percentage of persons harboring intestinal parasites at San Antonio and Maluno.*

Place.	No. examined.	Infected.		Infections.								Total infections	
				Single.		Double.		Triple.		Quadruple.			
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
San Antonio	3,310	2,819	85.16	1,529	46.19	1,133	34.23	151	4.56	6	0.18	4,272	129.06
Maluno	968	837	86.47	509	52.58	311	32.13	17	1.76	0	0.00	1,182	122.11
Total	4,278	3,656	85.46	2,038	47.64	1,444	33.75	168	3.93	6	0.14	5,454	127.49

Table V shows the relative frequency of the various parasites found at the two haciendas. The variations practically are negligible, excepting in the case of *Trichuris* which was found nearly twice as frequently at San Antonio as at Maluno; this is accounted for by the presence at the former place of the Visayans and the proximity of certain *cabecerias* to Ilagan *Central.* No infections with *Hymenolepis* or *Strongyloides* were found at Maluno.

TABLE V.—*Relative frequency of the various parasites found at San Antonio and Maluno.*

Place.	Number examined.	Infected.		*Ascaris.*		Hookworm.		*Trichuris.*		*Oxyuris.*		*Tænia.*		*Hymenolepis.*		*Strongyloides.*		Total infections.	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
San Antonio	3,310	2,819	85.17	2,082	62.90	1,788	54.02	296	8.94	51	1.54	45	1.36	5	0.15	4	0.12	[*]4,272	129.06
Maluno	968	837	86.49	571	58.99	538	55.58	46	4.75	13	1.34	14	1.45	0	0.00	0	0.00	1,182	122.11

[*] One trematode infection included.

Because the findings at the two places differ so slightly, they will be considered together in the following pages, excepting under the subject of geographic distribution, when conditions at San Antonio alone will be dealt with.

SEVERITY OF INFECTIONS.

The severity of the infections is measured by an impression of the number of ova seen in the specimens. Many of those with *Ascaris,* especially the ones occurring in children, were heavy, and those with *Trichuris, Oxyuris, Hymenolepis* and *Strongyloides* were light excepting a few cases of *Trichuris.* In one case the ova of the hookworm were very numerous, in a few instances not exceeding 15 ova per cover slip preparation were seen, while in the vast majority of cases, from 1 to 3 ova were present.

It is surprising to find practically only mild infections with the hookworm in a district where the parasite is found in over 50 per cent of the population. It has occurred to me that the flooding of the lowlands during the rainy seasons may be considered in this connection. Experiments have shown that fresh eggs of the hookworm die if they are placed in water, or if the culture medium (sand, or animal charcoal) is kept too moist. The same results are secured with the rhabditiform embryo of the parasite. On the other hand, the filariform embryo will live for a considerable time in water. Now the lowlands of the haciendas are flooded nearly every year. Sometimes they are flooded three or four times in one year and they remain so for three or four days at a time. It is possible that during the floods many of the eggs and embryos are killed, and that many others are washed away. If this were true it would tend to lessen the percentage of persons infected, and the severity of the infections with this parasite. It is also probable that the heavy rains themselves tend to clean the infested soil yearly. These suggestions are offered only as possibilities, not facts. In my opinion, not less than 95 per cent of the hookworm infections seen were distinctly mild in degree. If this is correct, it seems necessary to believe that some factor or factors are at work to cleanse the infested soil from time to time.

SEX.

The infections with *Hymenolepis* and *Strongyloides* are too few to admit of comparison. Males were found to harbor the hookworm and *Tænia* more frequently than females, whereas more females than males were infected with *Ascaris, Trichuris* and *Oxyuris,* as shown in Table VI.

TABLE VI.—*Sex distribution of infections.*

Sex.	Number examined.	Infected.		*Ascaris.*		Hookworm.		*Trichuris.*	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Males	2,290	1,999	87.29	1,349	58.91	1,432	62.53	179	7.82
Females	1,988	1,657	83.35	1,304	65.59	894	44.97	163	8.20

Sex.	*Oxyuris.*		*Tænia.*		*Hymenolepis.*		*Strongyloides.*		Total infections.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Males	23	1.00	35	1.53	3	0.13	3	0.13	3,024	132.05
Females	41	2.06	24	1.21	2	0.10	1	0.05	2,429	122.18

It will be noted that in the total infections present there were 132.05 per 100 males as against 122.18 per 100 females.

AGE.

The distribution of the parasites according to age is given in Tables VII, VIII, and IX. *Ascaris* was found to be more frequent in children than in adults, the highest percentage of infection (85.19) being in girls between 3 and 4 years old. Commencing with the group 7 to 9 years of age, there was a decided fall in the frequency of this parasite as age advanced, excepting a slight rise in females over 50 years old. *Trichuris* showed but slight variations as to sex and age. It was found more frequently in persons over, than in those under 15 years old. Infections with *Tænia* were met with more frequently in males over 50 years old, all of those with *Hymenolepis* occurred in persons under 16 years of age and *Oxyuris* was found oftener in individuals under 15. The hookworm occurred more frequently in males than females in corresponding age groups, excepting the small group of infants less than one year old.

TABLE VII.—*Age distribution of infections.*

Age (years).	Number examined.	Infected.		*Ascaris.*		Hookworm.		*Trichuris.*	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	20	3	15.00	3	15.00	1	5.00	0	-------
1	74	37	50.00	36	48.65	7	9.46	0	-------
2	184	138	75.00	132	71.74	25	13.59	6	3.26
3	162	146	90.12	135	83.33	31	19.14	6	3.70
4	153	126	82.35	116	75.82	38	24.84	6	3.92
5	172	155	90.12	141	81.98	47	27.33	11	6.40
6	161	141	87.58	126	78.26	58	36.02	14	8.70
7 to 9	375	337	89.87	270	72.00	202	53.87	33	8.80
10 to 14	495	443	89.49	346	69.90	308	62.22	38	7.68
15 to 30	1,100	980	89.09	671	61.00	741	67.36	104	9.45
31 to 50	955	789	82.62	472	49.42	591	61.89	76	7.96
Over 50	427	361	84.54	205	48.01	277	64.87	48	11.24
Under 15	1,796	1,526	84.97	1,305	72.66	717	39.92	114	6.35
15 and over	2,482	2,130	85.82	1,348	54.32	1,609	64.83	228	9.19

Age (years).	*Oxyuris.*		*Tænia.*		*Hymenolepis.*		*Strongyloides.*		Total infections.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	0	-------	0	-------	0	-------	0	-------	4	20.00
1	1	1.35	0	-------	0	-------	0	-------	44	59.46
2	3	1.63	0	-------	0	-------	1	0.54	167	90.76
3	1	0.62	0	-------	0	-------	0	-------	174	107.41
4	4	2.61	1	0.65	1	0.65	0	-------	165	107.84
5	6	3.49	0	-------	0	-------	0	-------	205	113.37
6	4	2.48	1	0.62	0	-------	0	-------	203	126.09
7 to 9	7	1.87	0	-------	2	0.53	1	0.27	515	137.33
10 to 14	6	1.21	2	0.40	0	-------	0	-------	700	141.41
15 to 30	13	1.18	18	1.64	2	0.18	1	0.09	1,550	140.91
31 to 50	13	1.36	23	2.41	0	-------	1	0.10	1,176	123.14
Over 50	6	1.41	14	3.28	0	-------	0	-------	550	128.81
Under 15	32	1.84	4	0.22	3	0.17	2	0.11	2,177	121.21
15 and over	32	1.29	55	2.22	2	0.08	2	0.08	3,276	132.40

TABLE VIII.—*Age distribution of infections (males).*

Age (years).	Number examined.	Infected.		*Ascaris.*		Hookworm.		*Trichuris.*	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	9	2	22.22	2	22.22	1	11.11	0	-------
1	48	21	43.75	20	41.67	4	8.33	0	-------
2	97	76	78.35	72	74.23	15	15.46	4	4.12
3	81	71	87.65	66	81.48	18	22.22	2	2.47
4	84	71	84.52	66	78.57	25	29.76	2	2.38
5	86	81	94.19	73	84.88	27	31.40	7	8.14
6	86	75	87.21	65	75.58	33	38.37	5	5.81
7 to 9	201	180	89.55	139	69.15	122	60.70	17	8.46
10 to 14	248	231	93.15	164	66.15	176	70.97	26	10.48
15 to 30	586	535	91.30	341	58.19	459	78.33	54	9.21
31 to 50	515	446	86.60	239	46.41	374	72.62	39	7.57
Over 50	249	210	84.34	102	40.96	178	71.49	23	9.24
Under 15	940	808	85.95	667	70.96	421	44.79	63	6.70
15 and over	1,350	1,191	88.22	682	50.52	1,011	74.89	116	8.59

Age (years).	*Oxyuris.*		*Tænia.*		*Hymenolepis.*		*Strongyloides.*		Total infections.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	0	-------	0	-------	0	-------	0	-------	3	33.33
1	0	-------	0	-------	0	-------	0	-------	24	50.00
2	3	3.09	0	-------	0	-------	0	-------	94	96.91
3	0	-------	0	-------	0	-------	0	-------	86	106.17
4	3	3.57	0	-------	0	-------	0	-------	96	114.29
5	1	1.16	0	-------	0	-------	0	-------	108	125.58
6	2	2.33	1	1.16	0	-------	0	-------	106	123.26
7 to 9	2	1.00	0	-------	1	0.50	1	0.50	282	140.30
10 to 14	2	0.81	2	0.81	0	-------	0	-------	370	149.19
15 to 30	3	0.51	12	2.05	2	0.34	1	0.17	872	148.81
31 to 50	5	0.97	14	2.72	0	-------	1	0.19	672	130.49
Over 50	2	0.80	6	2.41	0	-------	0	-------	311	124.90
Under 15	13	1.38	3	0.32	1	0.11	1	0.11	1,169	124.36
15 and over	10	0.74	32	2.37	2	0.15	2	0.15	1,855	137.41

TABLE IX.—*Age distribution of infections (females).*

Age (years).	Number examined.	Infected.		*Ascaris.*		Hookworm.		*Trichuris.*	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	11	1	9.09	1	9.09	0	-------	0	-------
1	26	16	61.54	16	61.54	3	11.54	0	-------
2	87	62	71.26	60	68.97	10	11.49	2	2.30
3	81	75	92.59	69	85.19	13	16.05	4	4.94
4	69	55	79.71	50	72.46	13	18.84	4	5.80
5	86	74	86.05	68	79.07	20	23.26	4	4.65
6	75	66	88.00	61	81.33	25	33.33	9	12.00
7 to 9	174	157	90.23	131	75.29	80	45.98	16	9.20
10 to 14	247	212	85.83	182	73.68	132	53.44	12	4.86
15 to 30	514	445	86.58	330	64.19	282	54.85	50	9.73
31 to 50	440	343	77.95	233	52.95	217	49.32	37	8.41
Over 50	178	151	84.83	103	57.87	99	55.62	25	14.04
Under 15	856	718	83.88	638	74.53	296	34.58	51	5.96
15 and over	1,132	939	82.07	666	58.83	598	52.83	112	9.89

Age (years).	*Oxyuris.*		*Tænia.*		*Hymenolepis.*		*Strongyloides.*		Total infections.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 1	0	-------	0	-------	0	-------	0	-------	1	9.09
1	1	3.85	0	-------	0	-------	0	-------	20	76.[illegible]2
2	0	-------	0	-------	0	-------	1	1.75	73	83.91
3	1	1.23	0	-------	0	-------	0	-------	87	107.41
4	1	1.45	1	1.45	1	1.45	0	-------	70	101.45
5	5	5.81	0	-------	0	-------	0	-------	97	112.79
6	2	2.67	0	-------	0	-------	0	-------	97	129.33
7 to 9	5	2.87	0	-------	1	0.57	0	-------	233	133.91
10 to 14	4	1.62	0	-------	0	-------	0	-------	330	133.60
15 to 30	10	1.95	6	1.17	0	-------	0	-------	678	131.91
31 to 50	8	1.82	9	2.05	0	-------	0	-------	504	114.55
Over 50	4	2.25	8	4.49	0	-------	0	-------	239	134.27
Under 15	19	2.22	1	0.12	2	0.23	1	0.12	1,008	117.76
15 and over	22	2.94	23	2.03	0	-------	0	-------	1,421	125.53

Two infants, one of 3½ months, the other of 9 months, were infected with *Ascaris;* another, of 9 months, with *Ascaris* and hookworm.

The number of infections per 100 persons was greatest in the age group 10 to 14 in the general findings and among the males and among females over 50, namely, 141.41, 149.19 and 134.27, respectively.

The percentages of persons infected with the various parasites are given by years up to the seventh year for the purpose of calling attention to the very high percentage of children, even infants, who harbor intestinal parasites. The results obtained show that infants between 1 and 2 years give an infection of 50 per cent with 59.46 infections per 100 examined. A year later the percentages rise to 75 and 90.76, respectively.

GEOGRAPHICAL DISTRIBUTION.

An attempt was made to study the geographical distribution of the infections among the thirty-three *cabecerias* of San Antonio. The percentages varied as follows:

TABLE X.—*Variation in the percentages of the parasites found at San Antonio according to cabecerias.*

Parasite.	Minimum.	Maximum.
	Per cent.	*Per cent.*
Ascaris	31.43	82.44
Hookworm	22.06	81.00
Trichuris	0.00	63.79
Oxyuris	0.00	5.56
Tænia	0.00	7.55

Since the *cabecerias* vary in population from 58 to about 200, it was to be expected that there would be considerable variation in the percentages of the various parasites found. As a rule the lower percentages were obtained in the smaller *cabecerias;* the higher ones in the larger. This particularly was true in regard to the findings for *Ascaris.* The occurrence of the hookworm seemed to be influenced chiefly by the nature of the sites selected for houses. Where the homes were located upon a rocky soil the infection with hookworms was less than where they were upon the lowlands. For instance, in *cabecerias* 2, 18, and 26, which are built on rocky soil, 23.60, 22.06 and 35.37 per cent were infected against 81.00, 70.59 and 67.09 per cent in *cabecerias* 14, 4 and 13, built on the lowlands. Since women are not found in the fields as often as men, it would be expected that a greater percentage of men would be infected if the infection took place in the fields (lowlands). This was found to be the case in the whole series (74.89 per cent against 52.83 per cent) and in the representative *cabecerias* under discussion as shown below.

TABLE XI.—*Hookworm findings in men and women in selected cabecerias.*

Number of *cabeceria.*	Group A. Located on rocky soil.					
	Men.			Women.		
	Examined.	Positive.	Per cent.	Examined.	Positive.	Per cent.
2	37	15	40.54	42	12	28.57
18	9	9	47.37	19	4	21.05
26	26	13	50.00	25	8	32.00
	Group B. Located on lowlands.					
4	25	24	96.00	29	18	62.07
13	26	20	76.92	25	14	56.00
14	40	37	92.50	28	23	82.14

The geographical distribution of infections with *Trichuris* was influenced by the 58 Visayans, 63.79 per cent of whom were infected with this parasite, and association with people in Ilagan *Central.* The Visayans had been at the hacienda about one year and undoubtedly carried the parasites into the valley with them. The whipworm was found more frequently among the persons living in *cabecerias* near them, than among those in other parts of the hacienda. The people who lived nearer Ilagan *Central* were more frequently infected with this parasite than those farther away, excepting the Visayans and their neighbors. The infections probably took place while the individuals were visiting in the town. These opinions are supported by the fact that Maluno, which has no Visayans and which is located at quite a distance from Ilagan *Central,* so that visiting is inconvenient, had fewer with *Trichuris* than had San Antonio.

The majority of the infections with *Tænia* occurred in *cabecerias* which are located near the mountains where it is the custom to hunt occasionally. During these hunting trips raw pork or deer meat is sometimes eaten.

MEDICAL SIGNIFICANCE.

While the investigation had, as one of its objects, the determination of the medical significance of the infections found, particularly those with the hookworm, its chief aim was to obtain statistics relative to the incidence of the various parasites. The great majority of cases were seen only once so that it was impracticable to study them clinically. Nothing can be said definitely regarding the influence of intestinal parasites at the haciendas, but nevertheless, general impressions as to the physical condition of the inhabitants were received. As a class, the people are anæmic and they have very little ambition. Many of the children present marked evidence of ascariasis. It was attempted repeatedly to select cases of infection with the hookworm before the microscopic examinations were made, but only unsatisfactory results were obtained.

It was not difficult to secure a history of symptoms which are frequently present in intestinal helminthiasis, such as nausea, vomiting, pain in various parts of the abdomen, constipation, diarrhœa, headache, dizziness, and restlessness, but it can not be stated that these symptoms were caused by the parasitic infections. Many factors are acting upon these people to lower their vitality and give rise to the symptoms mentioned. Climate, early marriage, rapid child bearing, poor food, excessive smoking, habitual use of alcoholics, and tuberculosis, all have their influence as well as the parasites. To determine the proportion of the symptoms due to helminthiasis would be a difficult problem, the solution of which would require most careful study extended over a considerable period of time.

The important question of the significance of hookworm infections among the Filipinos remains unanswered. A few years ago infections with this parasite were considered to be of importance, but during the past two years, there has been a growing tendency to attach less and less significance to them until now some believe them to be so mild that their influence is practically *nil*, or that the Filipinos enjoy a degree of immunity to the effects of the parasite. Such a change in opinion is neither a strange occurrence, nor one peculiar to the Philippine Islands. Beliefs regarding the significance of hookworm infections in the United States have varied. Too much importance was attributed to mild infections a few years ago, whereas, in my opinion there is an inclination to attach too little to them at present. It is the consensus of opinion among those who have worked with intestinal parasitism in the Islands that marked cases of the disease are rare among Filipinos. On the other hand, it has not been proved that the infections are so mild as to be of no importance from an economic point of view, or that of health. That intestinal parasitism has an effect upon mortality and morbid conditions in the Philippines is evidenced by the results obtained at Bilibid prison upon the institution of a routine examination and a routine treatment against the parasites. The Director of Health reports that a few years ago, when the Bureau of Health began its work at the prison, the annual death rate was 238 per 1,000. In response to the institution of sundry hygienic measures, the mortality fell to 75 per 1,000, and it seemed impossible to decrease the death rate beyond this figure. At this time the routine examination of the fæces for evidences of intestinal parasitism and the routine treatment of infected cases was begun, with the result that the death rate fell to 13.5 per 1,000 per annum. The routine work has been continued and the death rate has remained low. In addition to this general finding, the Director of Health tells me that the fall in the death rate occurred in brigade after brigade of the prison as the examination and treatment progressed from one to another; this is more convincing than the general findings that the fall in the mortality was due to the expulsion of animal parasites from the intestinal tract. Prior to the inauguration of this work deaths had rarely been attributed to intestinal parasites excepting *Amœba coli.* This is in keeping with the generally accepted opinion among medical zoölogists that the chief influence of helminthiasis is so to lower the vitality of the host that he is more susceptible to other diseases.

The statistical results of the examinations at Bilibid Prison were reported by Garrison. (Table III.) It is noteworthy that the hookworm ranked second in point of frequency. If the treatment for intestinal parasitism was an important factor in the remarkable decrease in the mortality at this prison, it is impossible to believe that the hookworm did no injury, as compared to that done by *Ascaris, Trichuris* and the other parasites present.

The fact should not be overlooked that Garrison found 142 infections with intestinal worms per 100 persons examined. Considerable work at Bilibid has convinced me that the hookworm is almost invariably associated with one or two, and sometimes more parasites. The results obtained at the prison must not be attributed to the expulsion of hookworms, but to the cleaning of the intestinal tract of parasites in general. It is quite possible that the hookworm occurring alone is of little significance and the same may be true of *Ascaris* and *Trichuris,* etc., but that when several infections occur in one individual, they are of considerable importance. I am persuaded that were 10 (instead of one) cover-slip preparations of the fæces of each case examined at Bilibid, fully 98 per cent of Filipinos entering the prison for the first time would be found to harbor one or more intestinal parasites; and that there would be very few single infections.

It seems incredible that the remarkable fall in the death rate at Bilibid Prison was alone due to treatment for intestinal parasites. The general hygienic conditions at the prison have been improved year after year since the Bureau of Health was given control of the health problems of the jail. In my opinion, some of the sanitary measures introduced contributed to the low death rate during the year in which the routine treatment for intestinal parasitism was inaugurated. On the other hand, the immediate fall in the mortality upon the institution of the routine treatment is quite too remarkable to be considered as a mere coincidence. The writer believes that the results obtained prove that intestinal parasitism is of no inconsiderable significance among the Filipinos.

Since parasites apparently contributed to the death rate at Bilibid Prison, it is permissible to believe that they are to be reckoned with in considering the morbidity; that is, the problem of intestinal parasitism is not only of medical but, also, of economic importance.

Confronted with the results obtained at Bilibid Prison and with those of the statistical studies of over 19,000 people in the Islands, approximately 85 per cent of whom, as the result of a meager examination were found to harbor one or more parasites, the problem of the proper disposal of human excreta is brought vividly to our attention. The fact that cholera, the various dysenteries, and other diseases would markedly be influenced by a proper disposal of the excreta does not subtract from the importance of the problem.

ACKNOWLEDGMENTS.

I was in the Cagayan Valley at a time when the people were very busy with their crops. The two haciendas are broken up into small *cabecerias,* and the tenants are provided with medical advice and treatment free of charge; thus my endeavors to make this study must have failed but for the coöperation of Señores Orros and Mesa, *administradores* of San Antonio and Maluno, respectively. I wish to acknowledge my indebtedness to them and their assistants for many courtesies.

Mr. Manuel Ramirez and Mr. Rafael Santos, fourth-year students in the College of Medicine and Surgery, University of the Philippines, rendered me valuable assistance in the examinations, and I wish to express my thanks to them also for their thorough, painstaking work.

A NOTE UPON ANTHRAX IN THE PHILIPPINE ISLANDS.

By W. H. Boynton.[1]

The existence of anthrax in the Philippines appears to have attracted very little attention. The only reference to it in print is by McMullen,[2] who was sent to the pueblo of Tagudin, Province of Ilocos Sur, in January, 1904, to investigate reports of a disease among animals the outbreaks of which antedated the American occupation. The disease occurred each year at the end of the rainy season and was most virulent at the onset of the outbreaks, killing animals in from two hours to three days after the first appearance of symptoms. Microscopic examinations of the blood from the viscera of animals dead of this infection revealed anthrax bacteria. Cultures were made in the Government laboratories in Manila.

In April, 1904, Doctor Lusk, veterinarian of the Second Cavalry, United States Army, reported the death of two mules from anthrax at Camp Wallace, La Union. These animals were of a pack train which plied between Camp Wallace and Benguet. The infection was supposed to have been contracted along the trail.

In addition to these observations, the correspondence files of the Bureau of Agriculture contain a few references to anthrax. The places mentioned are the townships of Bauco and Cayan, in the subprovince of Lepanto, Mountain Province; and Sual, Pangasinan. The existence of anthrax in Lepanto-Bontoc was questioned by a second veterinarian who investigated the matter. No evidence is at hand to show that any diagnosis in these outbreaks was confirmed by cultures. The records also show that three shipments of cattle from Hongkong were quarantined for anthrax.

ANTHRAX IN TAYTAY, RIZAL.

Dr. C. G. Thompson, in charge of the serum laboratory at Alabang, on the 14th of August, 1910, called the writer's attention to a smear preparation of blood made by Mr. Cattell, a live-stock inspector for the Bureau of Agriculture. This preparation was taken from a carabao which had died very suddenly in the vicinity of Taytay. Mr. Cattell stated that he made the smear immediately after the death of the animal. The staining material at hand was not of the best kind for distinguishing anthrax. However, upon microscopic examination, there was observed a large number of rather long, rod-shaped organisms with square-cut ends, some of them in chains, and others single, many being surrounded by what appeared to be capsules. It hardly seemed probable that these bacteria were putrefactive organisms, since the preparation was taken from the animal soon after death, but to be sure of the fact several guinea pigs were sent to Taytay, and instructions were given to the effect that if any animals there died in a similar manner a guinea pig should be inoculated with some of the blood, smear preparations made, a piece of the ear of the dead animal cut off, and both ear and smear preparations sent to the writer's laboratory at the Bureau of Science in Manila.

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[1] Pathologist, Bureau of Agriculture, Manila, P. I.

[2] A Preliminary Report on the Presence of Anthrax in the Philippine Islands. *Am. Vet. Rev.* (1904–1905), **28**, 935.

CASE I, *number 17.*—Carabao owned by Juan Villanueva, Santa Ana, Taytay, Rizal; died August 30, 1910. One guinea pig inoculated at 2.40 p. m., August 30, with blood taken from this animal after death; two smear preparations and a piece of the ear of the dead carabao were received on the morning of August 31.

The smear preparations were stained with an aqueous solution of methylene blue, recommended by M'Fadyean.[3] A large number of rod-shaped organisms with square-cut ends, occurring singly, in pairs and in chains, were present. Practically every organism was surrounded by an amorphous, violet or reddish-purple granular material. M'Fadyean states that he has never found this reaction in animals dead from diseases other than anthrax.

Smear preparations were made from blood procured from the ear. These smears were stained in a similar manner, and similar results were obtained. Agar cultures were made from blood obtained from the ear.

September 1: Guinea pig was found dead in the laboratory in the morning. Smear preparations made from the spleen, liver, and heart blood showed the presence of anthrax bacteria in stained preparations. Frozen sections made of the kidney, stained with carbol-fuchsin, showed the presence of anthrax bacteria in the capillaries between the tubules and in the glomeruli. Agar cultures were made from the spleen, liver, and heart blood. Agar culture made from the ear showed almost pure culture of anthrax bacteria characterized by the ground-glass appearance along the edge of the colonies, and showed, under the low power of microscope, long flexible filaments combining to form thread-like bundles.

September 2: Agar culture made from spleen, liver, and heart blood showed pure cultures of anthrax. An emulsion of some of the cultures obtained from the spleen was made in sterile water, and 1 cubic centimeter of this was injected subcutaneously into a guinea pig.

September 3: Guinea pig was found dead in the morning. Smear preparations from the spleen, liver, and heart blood showed the presence of large numbers of anthrax bacteria. Agar cultures were made from these organs.

September 4: Agar cultures made from spleen, liver, and heart blood showed pure cultures of anthrax bacteria.

Juan Villanueva owns another carabao, which, up to September 14, appeared to be in perfect health. He has not had any animals die suddenly before this one, except in 1901, when, he says, a carabao died with rinderpest. The animal which died of anthrax was purchased by him from dealers from Binangonan Malayo, Tayabas Province, in December, 1909. It was kept every day in a pasture called Libis, with many other carabaos. This pasture is situated between Taytay and Laguna de Bay.

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[3] A Peculiar Staining Reaction of the Blood of Animals Dead of Anthrax. *Journ. Comp. Path. & Therap.* (1903), **16**, 35.

CASE II, *number 19.*—Carabao owned by Saturnino Morales, Santa Ana, Taytay, Province of Rizal, died September 1, 1910. Guinea pig was inoculated on September 1, at 10.55 a. m., with blood from dead carabao. One smear preparation of blood and piece of animal's ear were received at the laboratory on the afternoon of September 1. Smear preparation of the blood, stained with aqueous methylene blue showed the presence of a large number of anthrax organisms giving M'Fadyean's reaction.

Smear preparations from ear of carabao stained with aqueous methylene blue showed the presence of large numbers of anthrax bacteria giving the same reaction. Agar cultures were made from blood of carabao's ear.

September 2: Agar cultures showed characteristic anthrax colonies, and cover-glass preparations showed the presence of anthrax bacteria.

Guinea pig died 11.30 a. m. Anthrax bacteria were found present in smears from spleen, liver, and heart blood, giving characteristic reaction to aqueous methylene blue. Frozen section of kidney stained with carbol-fuchsin showed anthrax bacteria present in capillaries of convoluting tubules, collecting tubules, and glomeruli.

Agar cultures were made from blood of spleen, liver, and heart.

September 3: Agar cultures made on September 2 showed pure culture of anthrax bacteria from spleen, liver, and heart blood.

This carabao was the only one owned by Saturnino Morales at the time of its death and when very young was brought from Antipolo. At the time of its death it was pastured every day along with a large number of other carabaos in a pasture place called Mahabang Sapa, which is separated from Libis by a shallow river.

CASE III, *number 23.*—Carabao owned by Victor Santos, barrio of San Juan, Taytay, Rizal, died September 8, 1910. Guinea pig was inoculated 8.35 a. m., and ear of carabao was received in laboratory about noon on the 8th.

Smears of blood from ear stained with aqueous methylene blue showed presence of anthrax organisms and gave M'Fadyean's reaction. Agar cultures were made from blood of ear.

September 9: Guinea pig was found dead and very much distended, showing that it probably had died on the evening of the 8th. Smear preparations made from the spleen, liver, and heart blood, stained with aqueous methylene blue, showed an enormous number of rod-shaped organisms. Some of them resembled anthrax, giving the characteristic reaction, while the others had the appearance of putrefactive organisms. Agar cultures were made from blood of spleen, liver, and heart.

Agar culture from ear gave practically pure culture of anthrax.

September 10: Agar cultures from spleen, liver, and heart blood showed mixed cultures; a few anthrax colonies were distinguished. Cover-glass preparations from these showed anthrax bacteria.

Victor Santos does not own any other carabao. The one which died was bought in Binangonan Malayo about two years ago. It was pastured every day along with many other carabaos in the pasture called Libis. Several years before a carabao owned by him died, but the nature of the death could not be ascertained.

CASE IV, *number 25*.—Carabao owned by Pedro Banals, San Gaibro, Taytay, Rizal, died September 13, 1910. The ear of the carabao was received in the laboratory early in the morning of the 14th. In smear preparations from the blood of the ear, stained with aqueous methylene blue, no rod-shaped organisms could be found. The only organisms seen were a very few micrococci. Agar cultures were made of blood from the ear.

September 15: Agar cultures showed no anthrax colonies, there being a few scattered colonies which resembled *Micrococcus pyogenes aureus*. Cover-glass preparations from several colonies stained with aqueous methylene blue showed the presence of a micrococcus. As far as can be decided from smear preparations and cultures, it would appear that this animal did not die of anthrax.

This man owns three more carabaos. These and the dead one were pastured every day in a pasture called Mapandon, with many other carabaos. He bought the carabao which died in San Mateo, Rizal, about three months before.

CASE V, *number 32*.—Carabao owned by Rufino del Rosario, Mapondon, Taytay, Province of Rizal; died on the evening of September 28, 1910.

The ear of the carabao received in the laboratory early in the morning of the 29th. Smear of blood from the ear stained with aqueous methylene blue showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

September 30: Agar cultures from ear gave practically pure cultures of anthrax.

This man owns five more carabaos, which, with the one that died, were pastured every day with many other carabaos, in Mapandan, a pasture ground situated on the opposite side of the town from Libis.

CASE VI, *number 33*.—Carabao owned by Mariano de los Reyes, San Isidro, Taytay, Rizal, died on the morning of September 29, 1910.

The ear of the carabao was received in the laboratory on the morning of the 30th. Smears of blood from the ear, stained with aqueous methylene blue, showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

October 1: Agar cultures from ear gave practically pure cultures of anthrax.

This man owns two more carabaos. These and the dead one were pastured every day with many other carabaos in a pasture called Lambac, a subdivision of Libis. He had owned this carabao several years.

CASE VII, *number 39*.—Carabao owned by Lazaro del Valle, barrio of San Isidro, Taytay, Rizal, died October 27, 1910.

The ear and two blood smears from the carabao were received in the laboratory on the afternoon of the 27th. Blood smear stained with aqueous methylene blue showed presence of anthrax organisms giving M'Fadyean's reaction. Agar cultures were made from blood of ear.

October 28: Agar cultures showed practically pure culture of anthrax.

This carabao was pastured on the 14th and 15th of October in Libis, but from the 15th of October to the time of its death the carabao was pastured in the fields of the barrio of San Isidro.

CONCLUSION.

1. From the results derived from the cultures, staining reaction, and animal inoculations, it is evident that anthrax exists in the vicinity of Taytay.

2. Since the animals, which were proved to have died of anthrax, were pastured in Libis, Mahabang Sapa, Mapandan, Lambac, and San Isidro. the infection is shown to be widely disseminated around the town of Taytay.

3. As it is almost impossible to procure definite information as to the number of animals and the manner in which they died in these places, one can not state whether the infection is recent or of long standing in this vicinity. The general opinion of the veterinarians is that it is of long standing, but has not been recognized as anthrax prior to this time.

REVIEW.

Primer of Sanitation for the Tropics. By John Woodside Rithchie and Margaret Anna Purcell. Cloth. Pp. x + 182. Illustrated by 94 figures. Price $0.60. Yonkers-on-Hudson: World Book Co., 1910.

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